A SYSTEM OF MEDICINE

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BY MANY WRITERS

EDITED BY

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PREFACE

I CAN no longer conceal from myself nor from my readers that the *System of Medicine* will not be contained within the five volumes at first proposed, one additional volume at least will be required. The relative lengths of the articles accord on the whole with the estimates, the absolute length of the series of articles will exceed the estimate.

That in length this work would exceed the *System* of Reynolds I was well aware; the advance of our knowledge since the date of publication of that work has been enormous: nevertheless I hoped that the greater number of pages in each volume, and the consignment of some matter to the *System of Gynæcology*, would have enabled me to complete the work in five volumes.

Our readers will not accuse us of diffuseness; there are few articles in which I have not ventured to take some liberties with my kind contributors, and to compress the matter as far as I might without loss. Indeed a gentle remonstrance, that this restraint has been carried quite far enough, has made itself heard here and there among our readers; it has been hinted, indeed, that one or two of the articles are a little too summary.

For the volume of new work on Infectious Diseases I was prepared; but I did not realise, nor can I deplore, the increase of our knowledge from almost every point of view; especially in respect of those scientific aspects of medicine which it has been my ambition in this work especially to set forth.

The justification of "specialism" in medicine is that by degrees the detail of it finds its way into common knowledge and skill, and is integrated in our Systems. *Thus, for example, I have endeavoured* in this volume to bring the diseases of the nose and throat into line with other parts of the general practice of medicine; but this means more and more liberal gifts of space. The study of the diseases of the nervous system, including the insanities, is advancing, likewise, from the remoteness of "specialism" into the broad way of general practice. A concise and lucid writer on these subjects, with whom I had agreed upon a certain space as sufficient for the chapter which he has undertaken, found, when he had collected and sifted all his materials, that no less than twice the space accorded to him is required. Now if many contributors find that their articles must transgress their confines by no more than a sixth or a fifth the volumes grow apace.

It has been and still is the purpose of the editor and of the publishers to produce a *System of Medicine* which shall be within the means of every practitioner; to this end much dialectical and historical matter has been rejected, and although, in order to maintain its authority, the work will exceed the limits at first assigned to it, they believe, nevertheless, that their purpose will be fulfilled.

As in previous volumes I have to express my cordial thanks for much kind assistance. I have had the advantage of Dr. Rolleston's co-operation as before; and I have also thankfully to acknowledge my obligations to Sir Felix Semon, who undertook the arrangement of the sections on Diseases of the Nose, Pharynx, and Larynx.

THE EDITOR.

CAMBRIDGE, *July* 1897.

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In order to avoid frequent interruption of the text, the Editor has only inserted the numbers indicative of items in the lists of "References" in cases of emphasis, where two or more references to one author are in the list, where an author is quoted from a work published under another name, or where an authoritative statement is made without mention of the author's name. In ordinary cases an author's name is a sufficient indication of the corresponding item in the list.

the mobility of the affected vocal cord, as a rule, is impaired at an early period also. As the disease progresses the hoarseness is changed to complete aphonia; but, on the other hand, the voice may return to some extent as the growth begins to break down, and thus temporarily the vocal cords are brought better together. In cancer of the epiglottis the voice may remain normal to the end; while in cases where the arytæno-epiglottic folds or the posterior surface of the cricoid cartilage are first attacked it may remain unaffected for a long time.

Pain may occur either at an early or at an advanced stage; but it is often insignificant, and we have observed cases in which this symptom was almost entirely absent throughout the whole course of the disease. Especially is this the case in the intrinsic variety. If present, it may radiate from the throat to the ear, the irritated fibres of the superior laryngeal nerve transmitting the irritation to the auricular branch of the pneumogastric nerve; yet this irradiation of painful sensation is by no means characteristic of malignant disease. Tenderness on pressure over the affected side of the larynx may often be elicited; and when the growth is considerable the larynx is sometimes found notably broadened in consequence of pressure from within. Pain on swallowing is sometimes observed in epiglottic growths, but is most marked when the disease is situated on the posterior wall of the larynx.

Cough, as a rule, is not a prominent symptom. Increased salivation from reflex irritation and increased secretion from the mucous glands are generally present, and, in consequence of the odynphagia, the saliva collects and, in the more advanced stages, may dribble out of the mouth. The secretion is at first frothy; later it is tenacious, semi-purulent, and streaked with blood. When the growth ulcerates, and especially when the perichondrium becomes affected, the secretion is fœtid, and a peculiar sickly, foul, musty odour is imparted to the breath. Respiratory obstruction depends on the size and situation of the growth. In the later stages of the intrinsic variety it is usually one of the most prominent symptoms. In the extrinsic variety it may result from the growth, if this be situated on the posterior surface of the cricoid cartilage, gradually destroying the muscular substance of the posterior crico-arytænoid muscles, and thus producing more or less complete paralysis of the abductors of the vocal cords. In the earlier stages slight hæmorrhages are common, and when ulceration of the growth has gone far, considerable hæmorrhages may occur.

Cancerous cachexia is sometimes absent throughout; particularly in intrinsic cases, owing to the arrangement of the lymphatics to which attention has already been drawn: but when the growth has spread to the pharynx the characteristic cachectic aspect is seldom long delayed. In large ulcerating growths, especially when extending into the œsophagus, the constant difficulty in deglutition may result in rapid wasting and loss of strength. Moreover, when the pharynx is involved, the lymphatic glands beneath the sterno-mastoid and the posterior cervical glands become enlarged.

Signs.—Malignant disease of the larynx, in its earlier stages, may appear, on the vocal cords as (i.) a single unilateral congestion; (ii.) a diffuse infiltrating growth, with a red, uneven surface; (iii.) a white, dirty white or reddish gray, broad-based, rarely pedunculated, semicircular or oblong wart, generally single and bearing a resemblance to a benign papilloma or fibroma; (iv.) an uneven fringe-like outgrowth from the cord. On the ventricular bands or arytæno-epiglottic folds and other parts of the larynx it may appear as a definite tumour, or as a deep grayish pink infiltration with a coarsely mammillated or uneven surface. Epiglottic growths are frequently more of a grayish or whitish pink, and may look almost fibrous in texture, but with uneven surface.

The disease may progress very slowly indeed at first, so that, even after the detection of a definite "wart," no appreciable alteration in size may have taken place after an interval of three or four months; on the other hand, rapid increase in size and early implication of neighbouring portions of the larynx is the more usual course, and points to malignity, especially if a growth which originally occupied the middle or posterior part of a vocal cord extends towards the arytænoid cartilages and posterior wall of the larynx. As the growth progresses it tends to ulcerate, at first superficially; and it readily bleeds. But deep ulceration is seldom long delayed: the floor of the ulcer is then covered with foul grayish muco-pus and débris tinged with blood. As the growth and ulceration extend, the cartilages often become involved; and a secondary perichondritis, which may proceed to suppuration and exfoliation of cartilages, not infrequently complicates the disease and may quite obscure its objective symptoms.

Sarcoma generally originates in the ventricular bands or epiglottis, or as an ill-defined, infiltrating growth the primary seat of which cannot be ascertained. The growth, if defined, is smooth, globular, and semi-translucent; but it may take the form of a grayish pink infiltrating tumefaction, with smooth but uneven surface. The rapidity with which it extends varies greatly in different cases.

The patient very rarely lives more than three years after the appearance of malignant disease of the larynx, if, that is, it be left to run its ordinary course; usually, indeed, the duration of life is considerably shorter. With advancing weakness and emaciation, and sometimes in a general cachectic condition, the patient sinks and dies; in many cases he is carried off by some intercurrent affection, such as bronchitis and congestion of the lungs, or by "foreign body pneumonia," due to the escape of particles of food or secretion through the distorted glottis into the lower air-passages.

Diagnosis.—The chief points which should attract our attention in cases of early malignant disease of the larynx are the age of the patient, the symptoms, especially that of hoarseness coming on without an obvious cause, the laryngoscopic appearances, the absence of general symptoms pointing to phthisis, syphilis, or gout (which, of course, do not *exclude* a concomitant cancer of the larynx), and—where possible—the histological character of portions of any growth removed for diagnostic purposes. The affections with which laryngeal carcinoma is most likely to be confounded are inflammatory diseases, laryngeal palsies, syphilis, tuberculosis, lupus, gout, benign growths, pachydermia laryngis, and perichondritis.

In those cases where malignant disease first manifests itself as a diffuse hyperæmia, it is distinguished from chronic laryngitis by its being unilateral; this character in itself would suggest to an experienced laryngologist the beginning of some serious affection, such as carcinoma, tuberculosis, or syphilis.

After a time in most cases increasing heaviness in the movements of the diseased vocal cord will be observed, which, taken in conjunction with the accompanying circumstances, the age of the patient, abnormal sensations or pain, and sensitiveness to pressure on the involved side, is a very suspicious symptom; and, in those cases in which it is present, it very usefully serves to distinguish malignant growths from benign neoplasms and pachydermia verrucosa. Sometimes this sluggishness of movement is seen at a very early stage of the disease, when the growth may be no larger than a pea. If this sign be absent from a case in which almost the entire vocal cord appears to be embedded in a papilloma-like mass, and in which age and other symptoms point towards malignancy, it is well to remember that the growth may have arisen from the ventricle of Morgagni; an origin which would explain the absence of this valuable sign. The growth, whether pedunculated or sessile, is generally surrounded by a circumscribed, diffused, dirty pink hyperæmia, which is often in striking contrast with the whiteness of the remainder of the cord and of the healthy one. Such growths may start from any part of the vocal cord, but—in contrast to the usual seat of benign papilloma—are very apt to originate from the middle or posterior thirds of the vocal cord, a site which when seen in patients over fifty years of age should always suggest grave suspicions. In colour they vary from an almost chalky white to a pink or dusky red; and their surface may be either smooth or granular, or mammillated. In a case observed by one of us (F. S.), the surface, its white colour apart, could best be compared to a newly-cut grass lawn; in another the appearances were those of a pedunculated angioma.

In other cases, again, the neoplasm is almost indistinguishable from a benign papilloma; yet a particularly fine branching of the individual papillæ, or the embedding of an entire vocal cord in a grayish white or reddish papilloma-like mass, or the appearance of a fringy papillomatous edge along its entire length, especially if one or more of these signs be observed in an elderly patient, will put the experienced observer on his guard. If, after removal of an apparently benign growth, rapid recurrence take place—especially if the recurring neoplasm be covered with an abundant growth of vegetations—or if the wound left by the removal of the whole or a portion of the growth fail to heal and present a sloughing, unhealthy aspect, malignancy should be strongly suspected. When the growth is larger in size the diagnosis is, of course, much easier. Large malignant growths would be distinguished from benign ones by their early ulceration and tendency to bleed. A gumma appears as a large, smooth, red tumefaction; and when it begins to ulcerate it breaks down and very rapidly disintegrates from the centre towards the periphery, so that a characteristic crater-like syphilitic ulcer results Syphilitic ulceration is usually easily distinguished from malignant by its relative painlessness and its rapid extension; sometimes, however, the differential diagnosis may present considerable difficulties, and a final decision may only be possible after long observation and the trial of iodide of potassium. Tuberculous disease of the larynx is accompanied by an anæmic appearance of the mucous membrane, while the tuberculous ulcers are superficial, often multiple, "mouse-nibbled" at the edges, difficult to define from the surrounding pale gray infiltration, and covered with pale grayish white débris. These ulcers tend to spread slowly and superficially rather than deeply. The concomitant pulmonary signs and bacteriological investigation will help to solve diagnostic difficulties; but it must be remembered that laryngeal cancer may coexist with pulmonary tuberculosis.

Definite malignant growths on parts of the larynx other than the vocal cords present similar features; while the general submucous infiltration, gradually involving various laryngeal structures, could only be mistaken for a sign of perichondritis from causes other than malignant.

The posterior third of the vocal cords and the interarytænoid fold are practically never the seat of benign growths; but these are the regions in which Virchow's pachydermia verrucosa is most frequently developed. The free movements of the vocal cords in the last-named disease, the crateriform depression on the summit of the tumefaction which forms in later stages of pachydermia, the relatively less pronounced hoarseness, and especially a history of chronic alcoholism, are strong points in the diagnosis of these excrescences, which, moreover, particularly in more advanced stages, tend to become bilateral.

It is a very good practical rule, in all cases of suspected malignant disease, to administer iodide of potassium for a while, even when there is no history of syphilis, in ten-grain doses at first, rapidly increased to thirty grains, three times a day. But we would again draw attention to the fact that mere subjective improvement after administration of this drug is not to be trusted; for patients, undoubtedly suffering from malignant disease, often declare themselves better after taking the iodide; we must, therefore, be guided by the changes in the size of the growth or infiltration.

Finally, the value of a microscopical examination of a removed fragment of a suspected growth has to be considered. When this reveals to a competent pathologist positive and unmistakable evidence of the malignancy of the growth—as in cases of squamous-celled carcinoma (epithelioma)—there is, of course, no room for doubt as to its character; but we cannot too strongly emphasise the importance of remembering that a mere negative verdict of the pathologist must not set aside clinical apprehensions otherwise well founded. The possibility of the growth being of a mixed character, or a papillomatous surface growing from a malignant basis, ought always to be remembered. In short, microscopic examination of fragments removed intra-laryngeally is a valuable but not an infallible aid to diagnosis. Every portion of the removed fragment should be cut into sections and each one carefully inspected; and if the examination reveal no characters of malignancy a further and deeper portion should be removed if the clinical appearances suggest any manner of suspicion as to its nature. However, there are but too many cases in which the disease appears in the form of a general smooth infiltration from which it is almost impossible, intra-laryngeally, to remove portions for microscopic investigation. In such cases the clinical observer must have the courage to form a definite diagnosis from clinical signs only.

Prognosis.—The prognosis varies enormously according to (*a*) the original situation of the growth; (*b*) the stage and extent of the disease at the time at which the patient comes under observation; (*c*) the patient's age and general health. Although a small intrinsic malignant growth in an otherwise healthy middle-aged patient allows of a much better prognosis (provided that immediate radical operation be consented to), than was considered possible a few years ago, the outlook in cases of extrinsic or very extensive intrinsic growth in very old patients, or in those whose general health has suffered from other causes, is still extremely grave.

The treatment may be considered under two headings, radical and palliative.

The radical treatment of malignant disease of the larynx may be said to have undergone a complete transformation within the last few years; for whereas attempts to extirpate the disease were so disastrous that they were rarely considered justifiable, the experiences of one of us (F. S.), who has been fortunate in having exceptional opportunities of treating malignant laryngeal growths surgically, and those of Mr. Butlin likewise, have yielded results which, when we remember the inevitable and speedy end of all such neoplasms when left to their natural course, are most gratifying. Taking as the basis of our remarks Semon's series of 103 cases seen in private practice between 1878 and 1894, we find that of 12 cases in which radical operations were undertaken no less than 7 ended in recovery, a percentage, that is, of 58·3 of the patients saved from a death otherwise inevitable.[1] In two of the fatal cases death was due to preventable complications not connected with the operation; otherwise the successful result might have been brought as high as 66·4 per cent. This gross result becomes even more important when the question of recurrence is considered. Hitherto it has been almost universally believed that even if radical operations in malignant disease be for the moment successful, a recurrence of disease within a comparatively short time, is an almost unavoidable contingency. The results in the above-mentioned cases give the most emphatic denial to this belief, for the duration of life in the operated cases was severally 7¼ years (patient dying of heart disease), 6 years,[1] 4 years, 3 years, 2 years, 1½ year, the last four patients being alive and well and free from recurrence. In the seventh case, in which recurrence appeared to be threatening when one of us last saw the patient, subsequent examination, as Dr. Hicks of Madeira informs us, did not prove this suspicion. The patient died suddenly ten months after the operation. At the necropsy a thick-walled abscess was found in front and extending to the left of the trachea. This had caused the dyspnœa and dysphagia from which he had been suffering during the last few months of his life, and which had given rise to the suspicion of recurrence.

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[1] Since the above was written I have performed four more thyrotomies for malignant disease of larynx, all of which were successful. The percentage of recovery in my 16 cases, therefore, now is about 69 per cent!—F. S.

Equally pleasing and surprising are the results from the phonatory point of view, the voice in all cases being fair and in some almost normal; although the whole of one side of the soft parts of the larynx had been removed.

It is when we come to the selection of cases which are suitable for operative treatment that we see the necessity for emphasising the importance of recognising the early symptoms of malignant disease of the larynx. Only in a very few exceptionally favourable cases can we undertake radical operations with any chance of success if the disease be not strictly intrinsic in its limitations. As regards the mode of the operative procedure, a few cases of successful extirpation through the mouth are recorded; but in early cases of intrinsic cancer this could be very rarely attempted with any prospect of success; nor even in such cases could we recommend the intra-laryngeal operation when we consider the infiltrating character of malignant growth, and the fact, proclaimed years ago by one of us (F. S.), and since corroborated by many observers, that when the larynx is opened the disease is almost always found to be much more extensive than was apparent on laryngoscopic examination. Thyrotomy, or subhyoid pharyngotomy, with removal of the growth by excision and partial laryngectomy, offers the best chance of getting rid of the whole disease.

The methods of performing these operations, and of carrying out the after-treatment, are beyond the scope of this work; for their full description the reader is referred to a paper published by one of us (F. S.) in 1894 (21).

Subhyoid pharyngotomy appears to be the most suitable procedure for removing growths of the epiglottis and arytæno-epiglottic folds.

Concerning the technique of total extirpation of the larynx and its after-treatment we must refer the reader to the text-books of surgery.

Palliative measures.—In cases which are unsuited for radical operation we have to rely on maintaining the patient's general health and strength by suitable tonic remedies, food and rest. If swallowing be painful, the food should be soft and bland: it is not well to urge patients to go on taking solid food when the local pain and irritation are increased thereby.

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[1] This patient has since died from an acute abdominal disease quite unconnected with the original laryngeal affection.—F. S.

With the supervention of respiratory obstruction, tracheotomy should be performed. Life may be prolonged a good many months in some cases by this operation, if the latter be not too long postponed; and in many patients there is a considerable improvement in other symptoms besides the dyspnœa. The low operation is preferable to the high, as the growth may spread down so as entirely to surround the tube. When ulceration has occurred, the use of antiseptic applications containing morphine is called for.

LARYNGEAL NEUROSES.—(I.) MOTOR NEUROSES

Introductory Remarks.—Whilst the vagus nerve by its superior laryngeal branch supplies sensation to the larynx on each side, and is the motor nerve to the crico-thyroid muscle, the recurrent laryngeal branches of the vagi supply motor innervation to all the other intrinsic muscles of the larynx. Hitherto the generally accepted view has been that the fibres of the recurrent laryngeal nerve are ultimately derived from the spinal accessory nerve through its communication with the vagus before it leaves the cranial cavity. According to the experiments of Grabower, Grossmann, and Walter Spencer, however, the recurrent nerve is derived from the vagus and not from the spinal accessory. This question is still an open one, and as yet we cannot give unqualified adherence to Grabower's statements. Moreover, his explanation of the cases in which paralysis of one vocal cord is associated with paralysis of the same side of the soft palate, of the tongue, and often also of the corresponding sterno-mastoid and trapezius muscles—an association which so clearly points to a nuclear lesion of the spinal accessory—has not quite satisfied us.

Exner's experiments on rabbits lead him to the conclusion that the thyro-arytænoideus internus is supplied by the superior laryngeal as well as by the recurrent, the thyro-arytænoideus externus by the superior and recurrent on each side, and the crico-arytænoidei laterales and postici by fibres from the superior and recurrent laryngeal nerves; while the depressors of the epiglottis are innervated by the superior laryngeal. It must be remarked, however, that clinical evidence is not in accord with Exner's views; and it is impossible as yet to regard them as a correct representation of the motor innervation in man.

The experiments of Semon and Horsley, corroborating Krause's investigations, demonstrated that there is in each cerebral hemisphere a bilateral cortical centre for adduction of the vocal cords (as in phonation); and that in the left hemisphere this centre corresponds with the speech centre, which in man lies in the anterior portion of the lower extremity of the ascending frontal convolution. Irritation or stimulation of either centre will produce bilateral adduction of the vocal cords, that is, spasm of the glottis; whilst destruction of one centre produces no corresponding paralysis so long as the other is intact. Thus in motor aphasia the vocal cords are not affected; and a unilateral cortical lesion has never been proved to cause unilateral paralysis of the opposite vocal cord, although French observers (Garel, Dor, Raugé, Dejérine) strongly maintain that this is possible; indeed they allege that it has been observed. It is impossible here to enter more fully upon this hotly-debated question; and we must refer those interested in it to a paper published by one of us (F. S.), in which it is fully discussed (22).

Semon and Horsley found a centre for abduction of the vocal cords in the cat lying close to the border of the olfactory (rhinal) sulcus; no abductor centre was found by these observers in any of the other classes of animals experimented upon, although the existence of such a centre in the cortex was almost certain from their discovery of a spot in each internal capsule, excitation of which gave rise to bilateral abduction of the cords. More recently, however, Dr. Risien Russell has discovered cortical centres for abduction in the dog also, which on unilateral excitation produce bilateral abduction of the cords; if, that is, the more powerful abductor movements have been to a certain extent abolished by previous section of the abductor fibres in the recurrent laryngeal nerve of one side. Abduction of the vocal cords was obtained from the anterior composite gyrus just in front of and below the adductor centre, and therefore a little in front of and below the anterior extremity of the coronal sulcus.

In further exploring the cortex Risien Russell found that on the anterior composite gyrus, below the abductor centre, there exists a focus, excitation of which results in what is described as a clonic abductor effect on the cords; in this action the cords were first brought into a position of moderate adduction which was followed by rapid short to-and-fro excursions.

On passing within the confines of Spencer's area for arrest of respiration, it was found that in the peripheral parts of this area there exist three foci, excitation of which affects the cords in different ways. The most anterior of these foci is responsible for arrest of the cords in adduction; that is, in the expiratory stage of their excursion. Excitation of the focus behind this, corresponding probably to Horsley and Semon's abductor centre in the cat, is followed by arrest of the cords in abduction, that is, in their inspiratory position; while stimulation of the most posterior focus, which is situated about the junction of the anterior composite and anterior sylvian convolutions, results in intensification with acceleration of the movements of the cords. Excitation of Mr. Spencer's chief focus for arrest of respiration on the olfactory lobe resulted in arrest of the cords in the position they occupy during expiration in dogs, and in the position they occupy during inspiration in cats.

In no instance in the whole of the experiments of Semon and Horsley, and Risien Russell, was there any indication of unilateral representation of the cords; on the contrary, excitation of the centre on either side produced an equal abduction effect on both cords alike. The experimental evidence on this point was corroborated by a remarkable case of Jacksonian epilepsy observed by one of us (W. W.), in which the patient, after a fit, while remaining perfectly intelligent, was the subject of complete motor aphasia, being unable to utter a single word, although he could produce inarticulate sounds; in him adduction and abduction of the vocal cords were found to be perfectly normal and bilaterally equal.

Another point of interest has been investigated by Risien Russell, namely, the inhibition of antagonistic muscles by electrical excitation of the cerebral cortex, on the lines adopted by Professor Sherrington with regard to antagonistic muscles in other parts of the body. This was tested by first dividing the fibres in both recurrent laryngeal nerves, leaving the abductor fibres intact, and then exciting the adductor centre with strong induced currents; but no evidence of inhibition of the abductor muscles was obtained.

Before entering on the discussion of the various forms of laryngeal motor disturbances, it will be well to refer to a law established by one of us (F. S.), namely, that in all progressive organic lesions of the centres or trunks of the motor laryngeal nerves the abductors of the vocal cords succumb much earlier than the adductors (8). Although a large number of such cases of progressive organic disease acting upon the whole of the nerve-trunk have been recorded, and publicly shown, in which the abductor muscles had undergone degeneration and atrophy, either alone or at any rate more advanced than in the adductors, not a single specimen has yet been demonstrated which, under similar conditions, exhibited the opposite order of events in the development of degenerative changes in the individual laryngeal muscles: all attacks made so far upon the law rest exclusively upon clinical observations, which are either incomplete, or are capable of an interpretation other than that adopted by their authors.

To explain this difference between the abductor and adductor muscles various hypotheses have been advanced. Thus Sir W. R. Gowers considered it might be a consequence of the advantage at which the most important adductor—the lateral crico-arytænoid muscle—works in comparison with the abductor (in so far as the former goes in at a right angle, the latter at a very acute angle towards the muscular process of the arytænoid cartilage), which renders the adductors capable of a longer resistance to disabling influences affecting the whole nerve-trunk. Grützner appears inclined to regard the adductors as belonging to the class of "white," and the abductors to the "red" class of muscles; and suggests that the difference in the muscles accounts for the difference in susceptibility to degenerative processes. Krause's suggestion is that the pathological process underlying the median position assumed by the vocal cords, under the conditions now referred to, does not consist in a primary paralysis of the abductor muscles followed by a paralytic contracture of the antagonists, but of a primary neuropathic contracture of all the muscles supplied by the recurrent, with preponderance of the adductors. He attempted to imitate experimentally the pathological process upon which during life the median position of the vocal cords most frequently depends—namely, the pressure of a tumour upon the motor nerves of the larynx—by fixing a piece of cork to the previously isolated recurrent laryngeal nerves, which were then replaced. After a few hours he first observed slight vibratory twitchings, afterwards a somewhat temporary median position, and after about twenty-four hours a permanent median position. This median position persisted without any change for two or three days, when it passed over into complete palsy. If the same experiment be performed on the pneumogastric nerve (it deserves special mention that Krause always operated on both sides), the vocal cords permanently assume the quiet position of expiration.

But in his explanation Krause did not distinguish between the sudden and intense irritation he had experimentally produced, and the slow and gradual increase of irritation by chronic pathological processes. The median position produced by him was probably correctly interpreted as an irritative phenomenon; and we do not deny that in a few human cases of acute character a neuropathic median position of the vocal cord may be of a similar nature. But in the enormous majority of cases in man a slow destruction of the nerve takes place, in which alterations of pressure, and with them irritative phenomena, can no doubt occur, though they are very frequently absent; and even in cases of the former kind the crico-arytænoid muscles succumb first. Krause fell into a self-contradiction when interpreting the atrophy of these muscles, as "atrophy due to inactivity"; since, according to his hypothesis, all the muscles supplied by the recurrent laryngeal, and therefore also the abductor, were supposed by him to be in a state of chronic irritation: moreover, in cases of slow pressure on nerves in other parts of the body—such as pressure on the facial nerve or on the brachial plexus, as in crutch-paralysis—we do not find contracture (that is, active primary muscular contracture as distinguished from secondary paralytic contracture), but paralysis. Further, from Semon and Horsley's experiments on different species of animals it appears that (*a*) the abductors are the first of all the laryngeal muscles proper to lose their excitability after death; and (*b*) that, when an animal is killed a week after thrusting a thread saturated with chromic acid solution through a recurrent nerve, the corresponding posterior crico-arytænoid muscle is the first to lose its excitability. Again, Risien Russell has also shown (*a*) that the abductor and adductor fibres in the recurrent laryngeal nerve are collected into several bundles, the one distinct from the other, and each preserving an independent course throughout the nerve-trunk to its termination in the muscle or muscles which it supplies with motor innervation; (*β*) that when the abductor and adductor fibres are exposed in the living animal to the drying influence of air under exactly similar circumstances, the abductor fibres lose their power of conducting electrical impulses very much more rapidly than the adductors; in other words, that they are more prone to succumb than are the adductors. Moreover, the fact, frequently observed, that in certain chronic central nerve affections—such as tabes dorsalis—paralysis of the internal tensors of the vocal cords (the thyro-arytænoidei interni) occurs with the vocal cords in the middle line, proves that the latter condition is due to primary paralysis of the abductors, and not to primary neuropathic contracture. Finally, the co-existence of other undoubted palsies with median position of one or both vocal cords, all of which lesions are due to one and the same cause, such as cerebral syphilis, renders it more than improbable that the laryngeal condition under such circumstances should be an irritative phenomenon.

Nor are we any longer quite in the dark as to the cause of the liability of the abductors to succumb. The fact discovered by Hooper, and corroborated and explained by Horsley and Semon, that ether has a peripheral and differential effect upon the laryngeal muscles which can be produced only by means of the circulation, the fact that the abductor muscles die sooner than the adductors, and the fact, demonstrated by B. Frankel and Gad, that gradual cooling of the recurrent laryngeal nerve paralyses the crico-arytænoideus posticus sooner than the glottis-closers—all these facts, taken together with the clinical and pathologico-anatomical experiences concerning the earlier destruction of the abductors in progressive organic lesions, imply that there is a positive difference in the biological composition of the laryngeal muscles and nerve-endings; whilst the fact that in central (bulbar) organic affections also, such as tabes, the cell groups of the abductors succumb earlier than those of the adductors, points to the probability that there are similar differentiations in the nerve-nuclei themselves. The phenomenon, hitherto obscure, thus finds its explanation in biological differences between the components of the laryngeal nerves and muscles. This constitutes an addition to our knowledge of the nervous morphology, but does not necessitate a revolutionary postulate such as is involved in the contracture hypothesis, namely, that the motor laryngeal apparatus possesses a pathology peculiar to itself. *We formerly knew that differences existed as* regards the irritability and power of resistance of the sensory and of the motor nerves, but we assumed complete equality among motor nerves. Now we have also learnt that differences of a more subtle kind exist among these nerves and the physiological conditions of the muscles they supply (2, 23, 24).

SPASMODIC AFFECTIONS.—Laryngeal spasms may be due to affections of the nerve-centres, nerve-trunks, or single nerve-twigs. With regard to the nerve-trunk affections, considering that stimulation of the peripheral end of the cut recurrent laryngeal nerve (that is, of all its fibres) results in adduction of the corresponding vocal cord, it is quite possible that, in cases of so-called "spasm of the glottis" of peripheral origin, not the adductors only, but also the abductors may be in a state of spasmodic contraction; the former, however, preponderating.

The various spasmodic affections may be conveniently divided into two groups:—(i.) Respiratory glottic spasm, and (ii.) Neuroses of co-ordination.

RESPIRATORY GLOTTIC SPASM.—**Laryngismus stridulus.**—*Etiology.*—This affection is almost invariably associated with rickets, and occurs chiefly in children from six months to two years of age, or up to the eighth or ninth year.

While the remarkable excitability of the nerve-centres in rickets disposes to the affection, the spasms are often excited directly by some reflex irritation in the alimentary tract, such as undigested food or parasites; or it may be due to post-nasal adenoids, or to such sources of excitation as teething, a pendulous epiglottis, or enlarged bronchial glands. It is sometimes directly brought on by emotion; and it is very likely that defective nutrition and consequent irritability of the cortical adductor centres may cause laryngismus (Semon and Horsley). This would also explain the "carpo-pedal" contractions, general convulsions, and so forth, which not rarely accompany laryngeal spasm in children, and which the authors just named consider as an overflow of energy from the irritated laryngeal adductor centre or centres to the neighbouring centres. The patients are often ill-nourished, unhealthy, micro-cephalic or hydro-cephalic children.

Laryngismus may arise as a complication of measles or whooping-cough, especially in children otherwise predisposed; and whooping-cough in particular leaves a strong disposition to laryngeal spasm for some months after its own disappearance.

Symptoms.—In a well-marked attack, after a few stridulous inspirations, short at first but gradually more prolonged, spasmodic closure of the glottis occurs, the respiratory movements of the chest and respiration ceasing absolutely. The child presents a most painful aspect, with the head thrown back, the neck forward, the eyes staring, the pupils contracted, and the countenance bearing an expression of extreme anxiety, at first flushed, then in a few seconds pallid or livid; the veins of the neck are swollen, and perspiration gathers on the face. The glottic spasm lasts from fifteen seconds to two minutes, and the glottis may remain closed till loss of consciousness or even death occurs. The attack, if not fatal, ends as it began with a few short stridulous inspirations, either continuous or intermittent, as in sobbing. In severe cases these symptoms are accompanied by spasms of the facial muscles, and by spastic, so-called carpo-pedal contractions; in these the thumbs are turned in and flexed on the palms and the fingers closed over them or rigidly extended; the carpal joints are turned inwards, the feet somewhat flexed and turned inwards. [*Vide* art. on "Tetany" in a later volume.] In some cases general convulsions supervene on these phenomena. In the less severe forms, the carpo-pedal spasms are absent and the symptoms less pronounced, the parents often speaking of the attacks as "passion-fits" or "holding the breath." Generally as soon as the attack is over the child resumes its play, and seems as well as ever. These attacks may occur very occasionally, or they may follow one another in quick succession; generally there are one or two attacks daily.

Prognosis.—In very severe cases death from asphyxia is by no means rare, and the prognosis should therefore be guarded, although the mean mortality of all cases is very small. From a therapeutic standpoint the prognosis is generally distinctly favourable, especially when there is a prospect of removing the underlying cause, as in rickety children who constitute the vast majority of the cases; yet some cases are very persistent, and, particularly in those which result from pressure by an enlarged bronchial gland, the attacks are liable to recur till the child has attained the age of eight or nine, or even more. In the "silent cases"—those in which there is no inspiratory stridor—the prognosis is especially grave.

The *diagnosis* of laryngismus stridulus rests upon the suddenness of the attack, the complete cessation of the respiratory movements at the height of the attack, the absolutely free intervals, and the absence of symptoms of inflammatory disease in the larynx, such as cough, hoarseness or aphonia, fever, and so forth.

Spasm of the glottis in adults is generally a reflex phenomenon brought about by irritation of a vagus or, in very rare instances, both recurrent laryngeal nerve-trunks by aneurysms or mediastinal growths and the like, or by direct irritation of the larynx by foreign bodies, neoplasms, adenoid hypertrophy of the lingual tonsil, an elongated uvula, and so on. Glottic spasm also occurs in certain lesions of the nerve-centres, as in the laryngeal crises of locomotor ataxia, in hydrophobia (in which, according to a very interesting observation made by Dr. Newton Pitt, the abductors of the vocal cords only appear to be affected by the spasm), tetany, and hysteria.

The *symptoms* are usually much less severe, though of the same character as in infants and children; they often amount to no more than a succession of stridulous inspirations.

In other cases, however, the spasm may be prolonged till consciousness is lost, or even life itself suspended. In very rare cases, according to some authors, there is a slight but constant spasm. In hysteria it may occur either in the paroxysmal or in the more continuous form: in the latter, which has also been termed functional inspiratory spasm, the vocal cords, instead of separating on intended inspiration, approach each other, remain together during the inspirations so that the air enters with difficulty and stridor through the narrowed glottis, and only separate to some extent during expiration.

Treatment.—As a rule, the spasm passes off spontaneously after a few seconds; but prompt measures should be taken to shorten the attack as far as possible by removing any tight garments, opening the window, placing the patient in the semi-recumbent position, and applying cold water to the face and head and smelling-salts to the nostrils, while the legs and body may be immersed in a hot bath. If asphyxia be threatening, tracheotomy should be performed without delay, followed, if necessary, by artificial respiration.

The general treatment depends on the exciting cause of the neurosis. Warm clothing, fresh air, simple diet, and avoidance of mental excitement or hard brain-work are of first importance. Fæcal accumulations, or intestinal parasites, when present, must of course be removed. Above all, if any indications of rickets are noted, treatment must be directed to overcome this condition by the administration of cod-liver oil, and especially of small doses of phosphorus. In strumous children the syrup of the iodide of iron and cod-liver oil will be useful. If the attacks recur frequently, small doses of bromide of potassium, belladonna, or chloral will tend to keep them off and render them less severe. In a case recently observed by one of us (F. S.) the use twice daily of a 2 per cent spray of cocaine, directed to the larynx, succeeded—probably by gradually diminishing the peripheral hyper-irritability—in causing attacks of very serious laryngeal spasm in a gouty adult to disappear completely within a fortnight (see p. 750).

NEUROSES OF CO-ORDINATION.—(*a*) *Choreic movements* of the vocal cords may accompany general chorea; and have also been noticed independently. We here refer to disorderly action of the cords in contradistinction to the glottic spasm with forced expiration in cases of "barking cough." In disseminated cerebro-spinal sclerosis a tremulous action of one or both cords, similar to the tremors of the limbs on intended movements, is sometimes present.

Functional inspiratory spasm has already been referred to as one of the forms of hysterical laryngeal spasm, the vocal cords coming together on inspiration, and separating but slightly on expiration. The symptoms in these cases are very similar to those of bilateral paralysis of the abductors; but when the vocal cords are watched by the laryngoscope during expiration they are occasionally seen to separate well. This affection appears to occur only in nervous or hysterical persons, though a minor degree of it is often witnessed in nervous people examined with the laryngoscope for the first time; the vocal cords in such cases are approximated instead of separated on attempted inspiration. Psychical treatment, bromide of potassium, the cold douche or intra-laryngeal faradic current usually effects a cure.

(*b*) *Nervous laryngeal cough.*—There is a condition in which spasmodic closure of the glottis appears in the form of separate, sudden, short contractions of the adductors, in association with similar contractions of other respiratory muscles, which results in an extremely loud, harsh, abrupt cough, the "barking cough of puberty" (Sir Andrew Clark). It occurs in young persons of both sexes. We have seen more men than women affected by it, and it is not limited to the period of puberty; it is most common between sixteen and twenty, but the ages of the patients vary from ten to twenty or more. The cough generally ceases during sleep, though not always; usually it is single, not a series of successive coughs, in which character it differs from the cough due to sensory laryngeal irritation; throughout the day it recurs persistently, even during rest. This nervous laryngeal cough is not associated with any demonstrable lesion, and the voice is not in any way impaired; there is no shortness of breath involving forcible inspiration after the cough. In fact, it is simply a sudden closure of the glottis, with a forcible expiration, due to affection both of the laryngeal and respiratory branches of the vagus. The general health is curiously little affected, and the cough often appears to be a much greater nuisance to the patient's family than to the sufferer himself.

This affection is really one of the "convulsive tics"; and is not in any way associated with volitional acts. It may last for weeks, months, or even years, but finally almost always ceases spontaneously. In young women it is often removed by the use of iron in strong doses for a few weeks.

Nervous laryngeal cough is very little amenable to ordinary treatment. The remedy which, with one single exception, has best answered in all the cases observed by one of us (F. S.) is a sea-voyage, which usually acts like a charm within a few days. Removal of the patient from home, a stay at the seaside, general sedatives, and the like, are not to be compared in efficiency to a sea-voyage, which ought to be urged upon the patient's friends, however great the difficulties. If a sea-voyage be altogether impossible, the internal use of bromides in large doses [sulphate of iron—ED.], and local cocaine applications may be tried.

(*c*) *Phonic spasm* (Dysphonia spastica).—This is a form of contraction of the adductors, originally described by Schnitzler, which is probably always allied to a similar contraction of the tensors of the vocal cords and of the thoracic expiratory apparatus, which only occurs on attempted phonation. The affection is analogous to writer's cramp, and one of us (F. S.) has seen a case of spastic aphonia associated with similar spasm of the masseter and orbicularis oris; another coexisted with writer's cramp.

This form of glottic spasm, like the preceding from which it differs in that it only occurs on attempted phonation, is rare. It is a disease of adult life and almost always occurs in highly-strung men who have to use their vocal organs professionally (especially clergymen), so that it may be classed amongst the "professional" neuroses. Occasionally, however, both men and women in robust health, and whose occupation is of a silent kind, may be attacked.

In its earlier manifestations the patient, after producing a few words, especially when using the voice in a professional capacity, such as preaching or reading the lessons in church, suffers from notable impairment or complete loss of voice. As the disease increases, any attempt at phonation results in spasmodic closure of the glottis, and the words are lost in fruitless attempts to force a current of air through the closed part. The voice under these circumstances assumes such a curiously oppressed character that even one who has never before seen a well-marked case of the disease may be enabled to diagnose subsequent cases from the particular timbre of the voice alone. Laryngoscopically the vocal cords are seen to act normally during respiration; but on attempted phonation the cords come into complete apposition; in fact, so forcibly are they adducted that they may seem to overlap one another, and one arytænoid cartilage may push itself in front of its fellow. The spasm lasts as long as attempts are made to speak; but as soon as voluntary effort at phonation ceases the glottis opens. Whispering is sometimes less difficult and may be possible. Respiration is free and noiseless.

To this class belong the cases described by B. Fränkel under the name mogiphonia, in which spasm with impairment or loss of voice occurs only in singing or attempts at public speaking, the ordinary conversational voice being unimpaired.

Treatment in these cases, in our experience, is almost always futile. All the remedies usually recommended in text-books fail—tonics, electricity, rest of voice, hydropathic treatment, sea-voyages, and so forth. The only method from which any improvement may be hoped for, and this in the earliest stages only, consists in rational breathing and elocutionary exercises: it is characteristic of these patients that they almost always attempt to pronounce or to read long sentences without taking an intermediate inspiration.

(*d*) *Laryngeal vertigo.*—There is a curious and rare form of spasm of the larynx, followed immediately by vertigo and loss of consciousness, to which Charcot originally applied this term. He considered it to be analogous to Menière's disease, the afferent nerve being, according to his view, the superior laryngeal. The views of its pathology differ widely: thus Krishaber regarded the vertigo as due to spasm of the glottis and arrested action of the respiratory muscles, and Gray looks upon the affection as a form of epilepsy. M'Bride explains the phenomena by the action of forced expiration into a closed glottis; he made experiments on the effect of forced expiration under these conditions, and found that sphygmographic tracings of the pulse showed a rapid and continuous diminution of the upstroke. This author states that in laryngeal vertigo there is a complete closure of the glottis, and thus the whole expiratory effort is felt, through the air contained in the lungs, by the alveoli, the large blood-vessels in the thoracic cavity, and the heart itself. As a result syncope—or a tendency to syncope—is produced, but almost at the same moment the spasm of the glottis relaxes and the attack is over.

The patient may seem to be in perfect health; or he may suffer from a catarrhal affection of the nasal passages. A tickling sensation in the larynx results in an effort to cough. This is immediately followed by giddiness and obscurity of vision, and the sufferer falls down in a state of unconsciousness which lasts a few seconds only, from which, as already stated, recovery is immediate and complete. The face is either pale or turgid—there may be slight twitchings of the face or limbs. In slighter cases consciousness may not be completely lost, the seizure terminating only with the occurrence of the vertigo. The attacks recur at intervals varying from a few days to months.[1]

As regards the treatment, the main indications are to improve the general health by rest and change of air, and by the administration of cod-liver oil and general nervine tonics such as iron, quinine, phosphorus, and arsenic; the tendency to spasm may be averted by bromides of potassium and similar remedies. Any catarrhal affection of the respiratory tract should be removed by appropriate treatment.

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[1] [illegible] least, [illegible] all [illegible]

PARALYSIS.—Motor laryngeal paralysis may be due to—

(i.) Degenerative changes in the nuclei of the laryngeal motor nerve-fibres in the floor of the fourth ventricle;

(ii.) Pressure on or destruction of spinal accessory fibres before their junction with the vagus nerve;

(iii.) Degeneration, injury or pressure on the vagus trunk, or its superior and recurrent branches;

(iv.) Functional neuropathic impairment;

(v.) Paralysis which, in its initial stages at any rate, may be reflex; although the nerve involved in a reflex paralysis generally undergoes actual organic changes; or finally,

(vi.) The paralysis may be myopathic in origin.

A. Paralysis of the muscles supplied by the recurrent laryngeal nerve.—The adductors and abductors of the vocal cords act by rotating the triangular arytænoid cartilages on their axes and by drawing them inwards and outwards respectively.

(i.) *Paralysis of the adductors of the vocal cords.*—Adduction of the vocal cords is brought about by the action of the crico-arytænoidei laterales, which arise from the sides of the cricoid cartilage, and pass backwards and upwards to the external angles of the arytænoid cartilages. By their contraction they cause inward rotation of the arytænoids on their axes, and the vocal cords approach in the middle line. But for perfect adduction the arytænoids must be brought into apposition by the arytænoideus and the thyro-arytænoidei muscles.

Paralysis of the adductors is almost invariably bilateral and due to functional disorders, probably cortical; as in hysteria, in cases of reflex uterine origin, and the like. Often it is a sign of general weakness of the muscles, as in phthisis, anæmia, or cholera; or it is caused by infiltration of the muscles, as in catarrhal conditions. The paralysis is very rarely complete; as a rule, there is only a greater or less degree of paresis of the adductors, and thus, laryngoscopically, the vocal cords may either remain widely divergent on attempted phonation, or more frequently are but insufficiently approximated and do not completely close the glottis: or if they do so, they promptly recede from apposition. The result of the deficient closure of the glottis is more or less complete aphonia. While in hysterical cases the voice is lost, the cough and sometimes the laugh are phonic, even if the voice has been lost for months or years; on the other hand, in the very rare cases due to local lesions, the cough is aphonic, or, rather, altogether impossible.

The onset of the affection is quite sudden in the hysterical cases, the duration most variable, from hours to years, and its ending perhaps as sudden as its onset. In cases of catarrhal origin, both the beginning and the passing off are, in accordance with the nature of the lesion, more gradual. If unilateral, the paralysis is nearly always due to local causes affecting the [illegible] on muscles. Unilateral adductor paralysis is [illegible] reported as having occurred from cold, syphilis, [illegible] and some cases of unilateral adductor paralysis ascribed to reflex influences from the nose are recorded (W. R. H. Stewart). The appearance presented by the larynx in the unilateral cases is not very characteristic, and is liable to be mistaken for total recurrent paralysis of one cord; therefore the laryngoscopic examination of these rare cases ought always to extend not merely to observation of the cords during quiet respiration and during phonation, but to inspiration as well, when further abduction will take place. It need scarcely be added that inasmuch as the healthy cord is widely abducted at the same time, the eye must be very expert to observe the increased excursion of the paralysed cord on inspiration; for it is the slightness of the outward movement of the cord—not merely the widening of the glottic chink—that must be detected.

The voice would be more affected in unilateral adductor paralysis than it is in complete unilateral recurrent paralysis, in which case the cord is in the "cadaveric" position; and the healthy cord can easily pass across the middle line to meet its fellow. In adductor paralysis the cord would be more or less abducted, or at any rate in the position of quiet respiration, and the healthy cord could hardly pass across and meet it.

The cases described by Solis Cohen under the name *apsithyria*, in which the patient not only loses the speaking voice but is unable even to whisper, are a form of functional paralysis of the adductors of psychic origin.

(ii.) *Paralysis of the abductors.*—The vocal cords are abducted by the crico-arytænoidei postici muscles, which, arising from the posterior surface of the cricoid cartilage, pass upwards and outwards to the external angles of the arytænoid cartilages. By their contraction the arytænoids are rotated outwards on their axes, and the vocal cords are abducted for the purpose of inspiration. It has been stated above that, in a case of incomplete organic paralysis of a recurrent nerve, those of its fibres which supply the abductor muscles are always first or pre-eminently palsied. In such cases there is at first of course only impaired abduction on the affected side; later, however, the unopposed antagonists of the paralysed muscles fall into a state of paralytic contracture and draw the vocal cord into the position of phonation, where it becomes immovably fixed. These remarks apply to both neuropathic and myopathic paralysis.

Abductor paralysis may be due to pressure on one or both recurrent laryngeal nerves, either by an aneurysm or tumour in the neck (particularly by goitres) or within the thoracic cavity—such as enlarged mediastinal glands, tuberculous thickening of the pleura covering the right apex of the lung, or by malignant disease of the œsophagus, or by a foreign body in it. It is also frequently due to central nerve-lesions in the medulla, or to implication of the vagus or spinal accessory nerves at the base of the brain, particularly in tabes dorsalis, and also in cerebral syphilis, disseminated cerebro-spinal sclerosis, bulbar paralysis, tumours of the brain, hæmorrhages into the bulb, or thickening of the dura mater.

Further, the paralysis may be due to the toxic neuritis of pneumonia, typhoid fever, diphtheria, scarlet fever, rheumatism, or influenza, or to the effects of lead, arsenic, or atropine; or again it may be myopathic in wasting diseases, or due to local myopathic impairments as in progressive muscular atrophy.

Finally, if there be pressure on the trunk of one pneumogastric nerve, the result may be bilateral paralysis of the abductors of the vocal cords; a reflex paralysis ingeniously explained by Sir George Johnson as the result of a centripetal irritation of the trunk of the vagus acting on the nervous centre, and through it upon the nerve-supply to the laryngeal muscles of the opposite side.

The left recurrent nerve is more frequently affected than the right; and the most frequent cause of this paralysis is aneurysm of the arch of the aorta; the right recurrent is more liable to compression by pleuritic thickening accompanying tuberculosis of the right lung and by aneurysms of the innominate, though it also may suffer from aortic aneurysm. The left recurrent nerve branches off from the left vagus on a level with the concavity of the aortic arch, and winds round it from before backwards to ascend to the larynx; while the right recurrent begins on a level with the right subclavian artery, around which it winds before passing upwards. Thus not only is the left recurrent very liable to be affected in the earlier stages of aneurysms of the aortic arch, even before there are any other manifestations of aneurysm, but as both the recurrent and the vagus above its recurrent branch have the longer course within the chest on the left side, there is also greater liability for the left cord to be affected by other intrathoracic tumours.

If any of these causes act on the recurrent nerve of one side, unilateral abductor paralysis results; while if the conditions obtain on both sides—that is, if there be a bilateral incomplete lesion of the bulbar centres, or of the trunks of both recurrent laryngeal nerves, or if there be pressure on one pneumogastric only with resulting reflex paralysis — bilateral abductor paralysis will result. Of course if the paresis result from interference with the vagus trunk above the superior laryngeal branch, anæsthesia of the larynx will be present, in addition to motor paresis. If the lesion be high up and due to a tumour, or to diffuse pachymeningitis, other cranial nerves, such as the spinal accessory, glosso-pharyngeal, and hypoglossal, may be involved.

In unilateral abductor paralysis the affected cord remains fixed in the median line, that is, in the position of phonation; and as the opposite cord is unaffected, respiration is not embarrassed unless the cause of the paralysis simultaneously produces direct compression of the lower air-passages, as in not a few cases of aortic aneurysm. Under such circumstances, that is to say, in the initial stages of all the severe lesions mentioned as "causes" which may implicate the laryngeal nerves—and indeed not rarely up to the patient's death—neither vocal nor respiratory symptoms need occur in adults: thus the laryngeal lesion, which may be of the greatest importance for the correct diagnosis of the whole case, will entirely escape notice unless it be a part of routine practice to examine all cases in which lesions of the laryngeal nerves could occur; whether there be symptoms pointing to the larynx or not.

In bilateral abductor paralysis both cords are defective in abduction on inspiration; and when the abductor paralysis is complete, the cords remain in or near the median position by the gradual supervention of paralytic contracture of the adductors, a very small chink only being seen between them. Laryngoscopically this looks like a continuous position of phonation. Inspiration is, of course, greatly embarrassed in complete paralysis; but fortunately bilateral abductor paralysis is often only partial; or while one cord is affected by complete abductor palsy the other is only partially palsied. Paroxysmal attacks of urgent dyspnœa, with characteristic stridulous inspiration, are prone to occur on slight exertion or mental excitement, and may at any time end in sudden and fatal asphyxia. In the intervals there is sonorous or stridulous inspiration, particularly in sleep; but expiration is free and the voice normal.

The prognosis of bilateral abductor paralysis is obviously very grave, and at any moment tracheotomy may be necessary. In progressive lesions the adductors may eventually become involved; and with the complete paralysis of the cords, which then assume the cadaveric position, respiration becomes less impeded, whilst the voice becomes impaired and finally quite aphonic. Such secondary implication of the adductors may not occur for several years; and, as the voice meanwhile is in no way impaired, bilateral abductor paralysis may exist without the slightest suspicion of such a disorder on the part of the patient; particularly in cases in which the patient is unable to make strong muscular efforts, as in the more advanced stages of tabes dorsalis.

(iii.) *Complete recurrent paralysis* (that is, involving all the muscles supplied by the recurrent laryngeal nerves) of the vocal cord results from lesions which are equivalent to a transverse section of the nerve affected. Any of the lesions mentioned as causes of abductor paralysis may give rise to complete recurrent paralysis. Probably abductor paralysis is always present for a longer or shorter time in the earlier stages of pressure on a recurrent nerve; but sooner or later the adductors are also involved.

If only one nerve is paralysed, the respiration is not affected, and the voice is either aphonic, hoarse, or sometimes almost normal when the healthy cord "compensates"—that is, crosses the median line in phonation to join its paralysed fellow; but it is apt, under such circumstances, to break into falsetto. During quiet respiration the larynx appears nearly normal, but in phonation the healthy cord is sometimes over-adducted and passes across the middle line to meet the paralysed cord, producing a peculiar distortion of the laryngeal image, the position of the glottis being oblique. The arytænoid cartilage on the paralysed side, being unsupported by its muscles, may be pushed aside so that it lies behind the sound and over-adducted arytænoid; and, like the corresponding vocal cord, lies at a somewhat lower level than on the sound side. In deep inspiration the paralysed cord and its arytænoid remain immobile in the cadaveric position, whilst the arytænoid on the healthy side passes farther back.

In bilateral complete recurrent paralysis, which is extremely rare, the vocal cords remain in the cadaveric position both during phonation and inspiration. There is no dyspnœa during rest, but there is complete aphonia. It is usually the result of pressure on both recurrent nerves; or represents the final stage of laryngeal paralysis due to central nerve-lesions, as in tabes, syphilitic nuclear disease, and the like; but it may be due to any of the causes enumerated under the heading of abductor paralysis.

(iv.) *Paralysis of the thyro-arytænoidei interni*, or internal tensors of the vocal cords, is usually bilateral; and is most frequently the result of over-straining the voice; or of catarrhal laryngitis, especially in anæmic and neurotic persons. The vocal cords are practically the tendons of the thyro-arytænoidei interni muscles which are inserted into their whole length. The function of these muscles is to render tense the free margin of the vocal bands; when therefore they are weakened, or paralysed, the vocal cords lose their normal flat appearance and become rounded and narrowed; thus they cannot approximate perfectly, and a narrow elliptical space, extending throughout the length of the glottis, is left between the cords during phonation, which consequently is weak and husky; or the voice may even be lost. The thyro-arytænoidei muscles are often paralysed in central nerve-lesions, and their paralysis is often associated with or follows next (F. S.) upon paralysis of the glottis-openers. It is, however, important to remember that some elliptic gaping of the vocal cords during phonation is by no means rarely seen in persons who are in full possession of their voice.

(v.) The *interarytænoideus* muscle may be paralysed alone in catarrhal conditions and in hysteria. The paralysis is always bilateral, and the voice is generally much impaired, or even quite lost. In these cases the anterior three-fourths of the vocal cords are seen to come together on attempted phonation, while a triangular chink is left between the vocal processes. Paralysis of the thyro-arytænoidei muscles may be associated with paralysis of the interarytænoideus, giving a characteristic double elliptic glottic chink.

B. Paralysis of the muscles supplied by the superior laryngeal nerve. —*Isolated paralysis of the crico-thyroid muscles.*—The function of the crico-thyroid muscles is to render the vocal cords tense on phonation; they are the external tensors of the vocal cords. Paralysis of the crico-thyroid alone is very rare. According to Mackenzie, it may be caused by cold or overstrain of the voice; and it is characterised by a wavy outline of the glottis with a slight depression of the central portion of the vocal cords in inspiration, and a corresponding elevation in expiration and vocalisation (see also Sensory Laryngeal Neuroses, p. 858). In unilateral paralysis of a crico-thyroid muscle the corresponding vocal cord stands on a higher level than its fellow. Mackenzie also pointed out that crico-thyroid paralysis can be detected by applying the finger to the crico-thyroid space on either side during phonation, when a want of tension will be felt.

For the treatment of paralysis of the superior laryngeal nerve and the muscles it supplies, see Sensory Neuroses.

Diagnosis.—The significance of laryngeal paralysis is of very considerable importance in medical practice; not only on account of the symptoms that may be produced, or the danger to life that may be involved in various forms of paralysis, but still more on account of the valuable aid to the diagnosis of many obscure intrathoracic or central nerve affections that may be afforded by a due appreciation of the pathological source of the laryngeal condition.

Even when the impaired movements of the vocal cords are undoubtedly due to local causes, it is necessary to distinguish between true neuroses, myopathic palsies, and the simulation of palsy by fixation or impaired freedom of action in the crico-arytænoid joint; or the impairment may be the earliest indication of early malignant disease in the cords or in their immediate neighbourhood. Local paralysis due to neuritis is generally of diphtheritic or rheumatic origin; myopathic paralyses mostly follow catarrhal inflammations. Mechanical fixation of the arytænoids by cicatricial contraction of the mucous membrane, after ulcerative diseases or injuries, may account for the immobility of the cords. Any thickening in the neighbourhood of the arytænoid cartilage, or abnormal distensions of the folds of mucous membrane, or tumefaction at the base of an immobile arytænoid cartilage, are in favour of mechanical fixation. In unilateral recurrent paralysis the arytænoid cartilage on the paralysed side may be displaced by the sound and over-adducted arytænoid cartilage.

Bilateral anchylosis is rather liable to give rise to error in diagnosis, inasmuch as it may so closely resemble bilateral recurrent paralysis; but complete paralysis of both cords (apart from anchylosis) is extremely rare.

Abductor or complete paralysis, whether unilateral or bilateral, may be the earliest symptom of a thoracic tumour—and especially of an intrathoracic aneurysm, of malignant disease of the œsophagus, intracranial disease, tabes, disseminated cerebro-spinal sclerosis, or general paralysis; even although all other signs be still absent. The possibility of any of these conditions being the cause of the paralysis should ever be present in the mind of the physician, who will endeavour to detect further indications of their existence. Points in favour of bulbar lesions are—(*a*) Persistent increased pulse frequency without any pulmonary affection or febrile disturbance to account for it; (*b*) Implication of both cords: but it is particularly to be noted that the fact of the paralysis being unilateral does not in itself indicate that the disease is peripheral; (*c*) Coexisting paralysis of the soft palate and tongue.

The **treatment** of laryngeal paralysis will depend upon the nature of the chief cause of the laryngeal condition. When it is due to pressure on a nerve-trunk or to central nerve disease, the prognosis is generally most unfavourable. In any form of organic laryngeal paralysis the chief indication is, if possible, to remove the cause of the mischief. When it is caused by syphilitic disease the usual antisyphilitic treatment is indicated. If enlarged glands or tumours are pressing on the nerve-trunks it may be possible to remove them (this applies particularly to goitre); but when the pressure is within the thoracic cavity, we can rarely hope to cure the paralysis by operative or medicinal treatment. In advanced bilateral abductor paralysis, since at any moment sudden and fatal asphyxia may arise, tracheotomy ought always to be proposed, not as a curative but as a prophylactic measure, pending the adoption of any further treatment by which we may hope to obtain a permanent cure, in which event the tube can be removed. A cure may be possible when the paralysis is due to pressure, as in goitre, syphilis, or diphtheria; but not when it is due to bulbar disease, as in tabes or labio-glosso-laryngeal paralysis: though in these bulbar cases complete recurrent paralysis may eventually supervene and render the tracheotomy tube unnecessary. In all cases in which the bilateral abductor paralysis is brought about by pressure within the thoracic cavity, the possibility of a second stenosis lower down, due to pressure on the trachea by the same tumour or aneurysm which is pressing on the nerve-trunk and causing the abductor paralysis, should be borne in mind; and in order to prevent disappointment the chances should be explained to the patient. A second seat of stenosis is probably present when there is marked expiratory as well as inspiratory stridor, and difficulty in respiration. But when the narrowing of the glottic chink is in itself sufficient to account for the dyspnœa, tracheotomy should be performed; and the low operation should always, if possible, be so chosen that the tube may be inserted below the compressing tumour, if it be in the neck; if it be in the thoracic cavity, it may be possible to pass a long flexible tube down the trachea and past the stenosis.

If the condition is due to maladies amenable to remedies—such as syphilis, or the neuritis of diphtheria or of cold—the general treatment will not be forgotten; while direct treatment of the paralysis itself, by local faradisation and hypodermic injections of strychnine (gr. $\frac{1}{30}$ gradually increased to gr. $\frac{1}{10}$), should be steadily pursued, in the hope that the conductivity of the nerve may not be wholly lost. In cases of functional paralysis of the adductors, due to excessive use of the voice in anæmic, overworked, or weakly persons, rest and tonic treatment must be enjoined. The patient must abstain from using the voice, live as regularly as possible, avoid all fatigue and mental worry, and take plenty of sleep, food, and open-air exercise, and a sufficiency of cold baths. Iron, strychnine, phosphorus, quinine, and arsenic and similar tonic remedies may be advantageously administered; and locally applications of mild galvanic or faradic electric currents must be applied to the region of the pneumo-gastrics. In cases due to inflammation, the usual remedies suited to laryngitis may be employed, as well as local faradisation.

In hysterical paralysis of the adductors, emotional effects, or anything that gives a shock to the system, will often produce a cure; and a similar result often follows stimulation of the larynx, as by inhalation of ammonia, the application of a laryngeal brush, and so forth. Nothing is so satisfactory, however, as local faradisation; and, though this may be given by applying an electrode to either side of the larynx externally, it is much more effectual if Mackenzie's endo-laryngeal electrode is used. The current, though not so powerful as to be actually painful, should be fairly strong at the outset; by timid handling the beneficial effects of the shock are often spoiled. One strong application is generally sufficient, but sometimes it has to be repeated once or twice.

In reflex paralysis the eccentric cause, such as uterine disorder for example, should be sought for and remedied.

Paralyses of the arytænoideus and crico-thyroid muscles, when due to cold or diphtheria, are often very obstinate; and local faradisation at frequent intervals may have to be continued over a long period.

LARYNGEAL NEUROSES.—(II.) SENSORY NEUROSES

ANÆSTHESIA.—The superior laryngeal branches of the vagi supply sensation to the mucous membrane of the larynx on each side; and loss of sensibility occurs when these nerves are paralysed. The loss of sensation may vary from slight diminution to complete anæsthesia; and the area affected may be on one side only, or may extend to the epiglottis or supraglottic portions of the larynx; or it may be complete, and invade the whole of the larynx and the upper part of the trachea. The anæsthesia may be due to peripheral lesions, as in diphtheria, syphilis, or injury to the vagus or superior laryngeal nerves; or it may be central in origin, as in bulbar paralysis, locomotor ataxia, general paralysis of the insane, apoplexy, after an epileptic fit, and generally, though in a minor degree, in hysteria.

But the superior laryngeal nerve also supplies motor innervation to the crico-thyroid muscles; and therefore in cases due to peripheral lesions, and sometimes in bulbar and other central nerve lesions, these muscles are paralysed at the same time. Obviously other motor laryngeal paralyses and lesions of other cranial nerves may coexist, according to the situation and extent of the disease.

The *symptoms* consist mainly in a tendency for mucus and food to enter the larynx. The mucous membrane of the larynx itself being insensitive, the particles of food often enter the lower air-passages. When the anæsthesia is complete and subglottic, the larynx does not react by reflex spasm upon the ingestion of food; so that the particles often enter the lower air-passages, and may either cause most violent cough—the tracheal mucous membrane having retained its reflex irritability—or may obstruct the passage and produce dangerous attacks of suffocation; or, again, may become impacted in the bronchi and give rise to pneumonia—the "Speisepneumonie" of the Germans. Hence it is also desirable, in all operations in which blood may enter the larynx, not to push the narcosis to the abolition of the cough-reflex.

In one-sided anæsthesia there is a tendency for mucus and saliva to collect on the insensitive side.

The *diagnosis* can only be made with certainty by touching the laryngeal mucous membrane in various parts with a probe under guidance of a laryngoscopic mirror, when defects of sensation and loss of reflex cough are readily detected. It is hardly necessary to emphasise the importance of noting any coexisting paresis or anæsthesia of the fauces, pharynx, or tongue.

The *prognosis* depends on the cause of the anæsthesia; in most cases the prospect of cure will be very remote. Post-diphtheritic anæsthesia tends to disappear spontaneously in the course of five or six weeks; but in all cases, so long as complete anæsthesia lasts, it is a very dangerous affection.

Treatment consists, in the first place, in special care in feeding the patient. In all forms in which anæsthesia is bilateral, food must be given by means of the œsophageal tube only, or by enema. Great care should be observed in introducing the tube, and it should be guided by the forefinger of the left hand lest it enter the open and anæsthetic glottis without producing cough. To be quite certain that the tube is in the correct position, the patient should be told to speak a word or produce a sound before the food is administered, as with the tube in the trachea phonation would be impossible.

Secondly, in those cases which are due to diphtheria, the faradic and galvanic electric current should be applied with one pole to the anterior wall of the pyriform sinus, near which the superior laryngeal nerve runs; and hypodermic injections of strychnine should be given. In syphilitic disease of the central nervous system iodide of potassium and mercurial inunctions are indicated.

HYPERÆSTHESIA, PARÆSTHESIA, AND NEURALGIA.—Increased sensitiveness of the laryngeal mucosa, tickling and pricking sensations or a sense of a foreign body in the larynx, burning sensations, pressure, pain, constriction, rawness, and other perverted sensations are commonly met with in hysterical, hypochondriacal, or anæmic patients. Sometimes these sensations are set up by an hypertrophied lingual tonsil impinging on the epiglottis, by caseous masses in the tonsillar crypts, or by pharyngitis; for any source of irritation in the pharynx or rhino-pharynx is usually referred subjectively to the larynx: in the majority of the purely neurotic cases, however, the laryngeal symptoms are associated with similar sensations in the pharynx (see Sensory Neuroses of the Pharynx, p. 761).

The result of laryngoscopic examination in these cases is generally negative, or at most reveals an anæmic condition of the mucosa. Hyperæsthesia is often a marked feature in gouty and rheumatic laryngitis; and a similar condition with perverted sensations is sometimes a premonitory symptom of tuberculous disease of the lungs; in all these cases, if there be the slightest suspicion of a tuberculous proclivity, the lungs should be examined by the physician. When associated with central nerve affections, such as tabes, the occurrence of laryngeal crises and the presence of abductor paresis and increased frequency of the pulse should suggest their real nature.

In these affections the indications are to improve the general health by nervine and tonic remedies, sea-bathing, and the like. If the pain be intermittent, and suggestive of neuralgia, quinine or croton-chloral-hydrate may be given, and locally a menthol spray may be used. Treatment, however, in these cases is generally most unsatisfactory, and on no account should the patient become habituated to narcotics. (See also Pharyngeal Sensory Neuroses, p. 761.)

III.—LARYNGEAL MANIFESTATIONS OF CHRONIC DISEASES OF THE CENTRAL NERVOUS SYSTEM

In *tabes dorsalis* the medulla oblongata is very often invaded; and among bulbar nerves the vago-accessory is by far the most frequently attacked. Hence the laryngeal nerves are very frequently affected. The various conditions that may arise are:—(i.) Sensory disturbances, such as anæsthesia, hyperæsthesia, paræsthesia, and the various abnormal sensations that precede or accompany laryngeal crises, such as tickling, constriction, inclination to cough, and in some instances anæsthesia. (ii.) Incoordination of the laryngeal muscles or of the vocal cords. The voice may be thick and jerky, or it may suddenly disappear after a few words have been uttered, as in dysphonia spastica. On attempted phonation, as observed by Krause, the cords may be suddenly adducted, then remain for a short interval in the semi-adducted position, and finally become adducted in the median line; during inspiration the cords, after being strongly adducted, are suddenly abducted to an extreme degree. Burger has drawn attention to the analogy between these irregular movements of the vocal cords, on attempted phonation or deep inspiration, and the ataxic movements of the lower extremities, in which the voluntary movements are very irregularly accomplished. (iii.) Laryngeal crises are frequently present in locomotor ataxia, particularly in its earlier stages, and may indeed constitute the earliest manifestation of this disease. In a considerable proportion of cases they are associated with abductor paresis, though they tend to become less severe and less frequent as the paretic condition becomes more marked. The onset of an attack is usually preceded by a sense of tickling in the larynx, with tendency to cough, quickly followed by a sense of constriction and dyspnœa due to the spasmodic closure of the glottis. A succession of abrupt coughs, resembling whooping-cough, continue till the patient feels almost asphyxiated; and are followed by inability to inspire, or by a long-drawn whoop, during which air is drawn into the chest with very great difficulty. The whole attack may last but a quarter of a minute, or may persist for five or ten minutes. Death from asphyxia is unusual but is not unknown. In some cases the laryngeal crises are attended by sneezing, vomiting, vertigo, pains in the chest and limbs, or even by general convulsions and loss of consciousness. (iv.) Paralysis, usually of the abductors of the cords, unilateral and bilateral. The symptoms of abductor paralysis are described on p. 853.

After abductor paralysis has lasted for some time it may be followed by adductor paralysis; but it should be noted that abductor paralysis may be the first, and for a long time the only demonstrable sign of tabes, and that adductor paralysis may not appear until the abductor paralysis has for many years been associated with the supervention of many definite symptoms of tabes. Thus one of us (F. S.) has met with a case in which the abductor paralysis had existed twelve years at least, and yet, though paralysis of the internal tensors—the thyro-arytænoidei—had occurred, the adductors were still unaffected. (The internal tensors, as already mentioned, are the muscles next in order to the abductors to succumb to progressive organic disease.)

In tabes, in association with abductor paresis, the pulse rate is very often persistently accelerated. This is due to the fact that the inhibitory nerve of the heart, like the motor nerves of the larynx, is derived from the accessory nucleus.

No necessary connection appears to exist between crises and paralysis. In a number of cases unilateral or bilateral palsy of the abductors, or complete recurrent palsy, are met with without any previous crises; in a second series no paralysis ensues, even after occurrence of frequent and severe crises; whilst in a third series both spastic and paralytic phenomena coincide in the same case. Should palsies occur, the law of the greater vulnerability of the abductors holds good. The spastic phenomena are probably due to an increased irritability of the adductor centres (F. S.). A peripheral stimulus conducted along the centripetal fibres of the superior laryngeal to those centres which, according to this hypothesis, are in a condition of increased irritability, does not set up a mere cough, as under normal conditions, but spasmodic coughing, spasm of the glottis, general convulsions, in short "a crisis." It also explains the influence of cocaine applications upon the larynx in laryngeal crises. The course of these palsies is generally slow and progressive, and the prognosis always unfavourable. The spasmodic attacks vary greatly in frequency. They may occur but two or three times in the course of years, or they may occur daily, or even two or three times a day. In some cases they occur spontaneously; they may come on suddenly during sleep, or they may be set up by slight forms of irritation, such as coughing, swallowing food or cold fluids, or on slight exertion.

In patients subject to laryngeal crises it is most important to observe the greatest caution in taking food. As a laryngeal crisis may come on suddenly, food should always be minced, lest a mass become impacted in the glottis and drawn in during the long inspiration; although the initial phase of coughing, if it occurs, would be a safeguard to the patient. All sources of local irritation, such as the ingestion of cold or very hot food, should be avoided. A cocaine spray or a solution applied to the larynx will often cut short an attack or a series of attacks; and one of us (W. W.) has seen marked relief from the inhalation of nitrite of amyl.

In *labio-glosso-laryngeal paralysis* anæsthesia of the larynx has been observed, but laryngeal crises are almost unknown. In several cases weakness of the glottis-openers has been noted. One of us (W. W.) observed bilateral paralysis of the internal tensors alone, without any abductor paresis; although the other usual features in the tongue and soft palate were well marked. Permewan has observed complete recurrent paralysis within nine months of the commencement of abductor paresis.

In *disseminated cerebro-spinal sclerosis*, laryngeal paralysis is very rare. One of us (W. W.) has observed tremor of the vocal cords on phonation, and coarse tremor on abduction. The slow monotonous tone, with jerky voice and scanning speech, is an early feature in most cases.

In *syringomyelia* both motor and sensory lesions, either unilateral or bilateral, are often present in the larynx; particularly the latter. Cartaz, analysing eighteen cases observed by French laryngologists, found that the larynx was involved in about 50 per cent of the cases. In some there was diminished tactile sensation in the larynx, amounting in a few to total anæsthesia; in others thermic sensation alone was affected.

Palsies of the muscles supplied by the recurrent laryngeal nerves have also been observed, the abductors failing first. In total paralysis of long standing the vocal cord or cords are said to become atrophied.

Laryngeal crises do not appear to have been observed.

In *general paralysis of the insane*, Permewan concluded, from an examination of thirty-four cases, that in at least 20 per cent there is more or less marked abductor paresis. His observations again confirmed the general truth of the law laid down by one of us (F. S.) as to the special liability of the abductors to succumb in organic disease.

FELIX SEMON.
WATSON WILLIAMS.

REFERENCES

1. BOSWORTH, F. *Diseases of the Nose and Throat.* New York, 1897.—2. *Brain*, parts lix.-lx., 1892.—3. BURGER. *Die laryngealen Storungen der Tabes Dorsalis.* Leiden, 1891.—4. CHAPPELL, W. F. *Amer. Med. Surg. Bull.* Jan. 18, 1896.—5. CHIARI and RIEHL. "Lupus des Keblkopfer," *Vierteljahresschrift fur Dermat. und Syph.* Wien, 1882.—6. DELAVAN, BRYSON. "Recent Advances in the Surgical Treatment of Malignant Disease of the Larynx," *Trans. Amer. Laryng. Assoc.* 1896. —7. FRENCH, T. R. "Laryngeal and Post-nasal Photography," *Trans. Amer. Laryng. Assoc.* 1896.—8. GOTTSTEIN. *Die Krankheiten der Keblkopfer.* Leipzig and Wien, 1888.—9. *Internationales Centralblatt für Laryngologie*, etc., vols. v., vi., 1888-89.—10. KIRSTEIN. *Autoscopy of the Larynx and Trachea*, 1897.—11. KRISHABER. "La Pathologie de la Phthisie Laryngée," *Trans. of the Internat. Med. Jour.* 1881, London, p. 208.—12. MACKENZIE, MORELL. *Diseases of the Throat and Nose*, vol. ii. London, 1884.—13. M'BRIDE. *Diseases of the Throat, Nose, and Ear.* Edinburgh, 2nd ed.—14. NEWMAN, D. *Malignant Diseases of the Throat and Nose.* Edinburgh, 1892.—15. Perichondritis of the Larynx, a Discussion on, at the Brit. Med. Assoc. Meeting at Leeds, 1889, *Brit. Med. Jour.* 1889, vol. ii. p. 588.—16. PRZEDBORSKI. "Ueber Lahmungen der Keblkopfmuskeln beim Unterleibs und Flecktyphus," *Sammlung klin. Vort.* Leipzig, 1897, No. 182.—17. SAALFELD. "Ueber die sogenannte Pharyngitis granulosa," *Arch. pathol. Anat.*, etc. Berlin,

1880, lxxxii. p. 147 *et seq.*—18. Schrotter. *Behandlung der Larynx-stenosen.* Wien, 1876.—19. Semon, Felix. "Die Nerven Krankheiten in Larynx und Trachea," Heyman's *Handbuch der Krankheiten des Halser und der Nase.* Berlin, 1897. [In the Press.]—20. *Idem.* "On Mechanical Impairments of the Functions of the Crico-Arytænoid Articulation, with remarks on Perichondritis of the Laryngeal Cartilages," *Med. Times and Gazette*, vol. ii. 1880.—21. *Idem.* "The Radical Operation for Malignant Disease of the Larynx," *Lancet*, Dec. 15, 22, 29, 1894.—22. *Idem.* "The Study of Laryngeal Paralysis since the Introduction of the Laryngoscope," *Brain*, 1892.—23. Semon, Felix, and Horsley, Victor. "An Experimental Investigation of the Central Motor Innervation of the Larynx," *Phil. Trans. of the Royal Society*, vol. clxxxi. (1890), pp. 187-211.—24. By the same Authors. *On an apparently Peripheral and Differential Action of Ether upon the Laryngeal Muscles.* 1886.—25. Simpson, W. K. H. "The Sequelæ of Syphilis in the Pharynx and their Treatment," *Trans. Amer. Laryng. Assoc.* 1896.—26. Sota, de la. Burnett's *System*, vol. ii. p. 436 *et seq.*—27. *Idem.* "Lupus and Leprous Laryngitis," Burnett's *System*, 1893, vol. ii.—28. *Trans. Pathol. Soc. of London*, vol. xlii. p. 37; vol. xliv. p. 26.—29. Turner, W. Aldren. "The Central Connections and Relations of the Trigeminal, Facial, Glosso-Pharyngeal, Vago-Accessory, and Hypoglossal Nerves," *Jour. of Anatomy and Physiol.* 1895, vol. xxix. pt. i. p. 1.—30. Watson Williams, P. *Diseases of the Upper Respiratory Tract; the Nose, Pharynx, and Larynx.* Bristol, 1897.

F. S.
W. W.

The following table, compiled by one of us (W. W.), summarises the main points of distinction between several of the diseases of the pharynx and fauces :—

Carcinoma.	Sarcoma.	Chancre.
Symptoms. — Dysphagia is always an early symptom, and pain is considerable and persistent, but of gradual onset. Increased pain on swallowing becomes so great as to prevent the patient taking food. Saliva accumulates in the mouth. Early and well-marked cachexia, and rapid loss of flesh. *Physical Signs.*—Carcinoma always presents an enlargement with superficial irregularity of surface, which is light pink or bluish, and soon ulcerates with granular fissured surface, hard elevated margin, general cartilaginous hardness and fixedness. Ulceration not very depressed, covered with fœtid mucopus. Early infiltration of neighbouring glands. Hæmorrhage frequent and often profuse, sometimes fatal. Generally unilateral.	*Symptoms.* — Difficulty and pain in deglutition, sometimes very slight, and, until ulceration occurs, is chiefly mechanical. Saliva accumulates and dribbles from the mouth Loss of flesh generally rapid. *Physical Signs.* — Sarcoma attains considerable dimensions before ulceration commences. The growth is red, fleshy-looking, and soft, surrounded by a well-marked bright red areola. Spreads to neighbouring regions and externally to the neck,—especially rapid is the extension of round-celled sarcomata. Hæmorrhage is frequent and sometimes fatal Generally unilateral.	*Functional Symptoms.*—The first symptom is a stinging pain in the tonsil, but with little pain on swallowing, which is never so difficult as in cancer or in tertiary syphilis. Cancer occurs in late middle life, but sarcoma may also occur in the young; chancre generally in young adults. *Physical Signs.*—The surface is very red, but there is always a well-defined erosion, with sharply-cut margin from the commencement. Induration or even stony hardness. The submaxillary glands early enlarged Like cancer and tertiary syphilis, and unlike secondary, it is unilateral. No hæmorrhage, only streaks of blood. No emaciation, early appearance of secondary rash, etc. Responds well to treatment
Syphilis, **Secondary and Tertiary**	**Tuberculous Ulceration.**	**Acute Tonsillitis.**
Symptoms.—Often no pain whatever, and swallowing often difficult, never impossible. Wasting and cachexia in proportion to the difficulty in taking nourishment, and not very pronounced. No salivation. In secondary syphilis of the tonsils and fauces there is generally bilateral deposit of mucous patches and superficial ulceration, with well-marked purplish areola. In tertiary syphilis the tonsils are unilaterally affected by a deep perforating ulcer. The margins of the ulcer are often undermined, and overhang the deep-lying ulcer, the floor of which is covered with necrotic tissue. The sympathetic glandular enlargement is slight, and not painful as in cancer. Hæmorrhage slight or absent. The rapid improvement under antisyphilitic remedies is always a valuable sign.	*Symptoms.*—Swallowing is always very painful, and loss of flesh rapid, with nocturnal rise of temperature, and a general well-marked tuberculous cachexia is always present. There is early and rapid infiltration of the parts around, with very early tendency for fluids to return through the nose on swallowing. *Physical Signs.* — General pallor, with diffuse infiltration of the affected region. Early superficial, irregular, mouse-nibbled ulceration, with gray débris. In the earlier stages the deposits of miliary tubercles are very characteristic ; these ulcerate and coalesce. No inflammatory areola. Hæmorrhage generally absent. Usually concomitant disease of larynx and lungs.	*Functional Symptoms* — Pain very marked from the commencement, great tenderness and difficulty in swallowing. Generally some rise in temperature Usually both tonsils affected, though one after the other. *Physical Signs.*—Characteristic redness and inflammatory infiltration. Lacunar exudation, but no ulceration. May proceed to suppuration *Chronic abscess* of the tonsil may be diagnosed by incision and discharge of pus. Responds well to treatment.

F. S. and W. W.

Pharyngeal Neuroses.—(*a*) *Motor Neuroses.*—The motor neuroses of the pharynx may be conveniently divided into spasmodic neuroses and paralyses.

Spasm of the pharyngeal muscles is nearly always a functional disorder. It is a rare affection, interfering with deglutition, generally met with in nervous and hysterical patients. It may occur in association with various acute inflammatory processes, such as acute tonsillitis. Spasm of the pharynx is a prominent symptom in hydrophobia, and has been observed in a case of cerebral tumour. Courmont records a case of tonic spasm in tabes. Clonic spasm of the levator palati gives rise to a peculiar clicking sound audible to the patient and those around. The cause is obscure; but by some observers it is regarded as a reflex neurosis, and therefore any possible source of irritation should be removed.

In some cases local application of the galvanic current has proved useful in relieving spasm. When due to hysteria or associated with neurasthenic constitutional states, nervine tonics, rest, and change of air are indicated.

Paralysis.—The experimental results of Horsley and Beevor show that the soft palate and uvula, the levator palati and the pharyngeal constrictors are innervated by the spinal accessory fibres in the pharyngeal plexus, and not by the vagus. The tensor palati is supplied by the fifth nerve. Thus paralysis of the soft palate may be caused by central nerve lesions involving the spinal accessory, or by peripheral neuritis and pressure on the nerves to this region, or the paralysis may be myopathic.

The paralysis is generally unilateral, but may be bilateral.

Paralysis of the palate from bulbar disease may be due to acute or chronic myelitis involving the spinal accessory nuclei, to bulbar apoplexy or embolism, to tumours, or to basilar meningitis.

Acute bulbar paralysis is characterised by the sudden onset of giddiness, headache, and sometimes vomiting, with unsteadiness of gait, but with no loss of consciousness. The voice becomes nasal and thick, and, the lips and tongue being involved, articulation is difficult. The dysphagia increases, and finally respiration becomes irregular, and the pulse small and frequent from the progressive implication of the various bulbar nuclei.

Chronic bulbar or glosso-labio-laryngeal paralysis generally begins in the tongue; then the lips, velum palati, and pharyngeal constrictors are involved; and very often the abductors and internal tensors of the vocal cords likewise. Speech becomes nasal in tone, articulation very imperfect, and swallowing very difficult, and liable to result in the food passing into the larynx. The vago-accessory nuclei being concerned, the pulse is often persistently frequent, respiration may become shallow and irregular, and attacks of periodic dyspnœa are not uncommon towards the end. Unilateral paralysis of the tongue, palate, and larynx, first described by Dr. Hughlings Jackson, is of special interest from the light it throws on the innervation of the soft palate; inasmuch as it implies that the motor innervation of the organ is supplied by the accessory in agreement with the experiments to which we have referred above. Moreover, in several cases the trapezius and sterno-mastoid were also paralysed, and thus both branches of the accessory were affected, whilst there was no symptom pointing to an affection of the vagus.

Post-diphtheritic neuritis is the most common cause of palatal paralysis. A similar condition may probably be caused by membranous sore throat not associated with the Klebs-Löffler bacillus, and from acute lacunar tonsillitis.

Paresis of the palate and constrictors of the pharynx may be due to hysteria, or to general weakness in the anæmic and debilitated.

The *symptoms and signs* of paralysis vary as it is unilateral or bilateral. When the lesion is unilateral, the uvula is drawn towards the healthy side, and the velum palati is drawn down by the palato-pharyngeus and palato-glossus on that side; if bilateral, the velum palati hangs loosely and does not respond to local stimulation, the voice is nasal, and fluids escape by the nose during deglutition. As the paralytic condition of the pharyngeal constrictors becomes better marked, deglutition gets more and more difficult, and the difficulty in swallowing fluids is always greater than for solids, in contradistinction to the difficulty in swallowing due to obstruction, when, as we should expect, it is first noticed, and is always more pronounced in the swallowing of solids.

It is necessary to distinguish from true pharyngeal paralysis the very similar appearances which may result from inflammatory exudation and mechanical interference with the movements of the soft palate resulting from syphilis and other forms of local disease.

The view that paralysis of the palate is due to and accompanies paralysis of the facial nerve has nowadays lost most of its former adherents.

The *treatment* of pharyngeal paralysis will, of course, depend on the causes. In many cases local treatment is obviously of no use whatever. Post-diphtheritic paralysis should be treated by hypodermic injections of strychnine and local faradisation.

(*b*) *Sensory Neuroses.*—*Anæsthesia*, partial or complete, may be unilateral or bilateral. The commonest cause is diphtheria; but it may occur in hysteria, bulbar paralysis, and in insanity; it is also produced by pressure on a glosso-pharyngeal nerve by tumours near the exit of the nerve from the skull, or by intracranial tumours, gummas, etc. It is nearly always associated with neuroses of sensation and paralyses of the velum and larynx.

Hyperæsthesia and paræsthesia of the pharynx are often met with, apart from any organic disease, in anæmic and neurotic patients; but in many cases some slight affection of the tonsils or granular pharyngitis is the source of a discomfort altogether out of proportion to the cause. Very similar painful or uncomfortable sensations in the pharynx are often found in gouty patients, in the early stages of pulmonary phthisis, of cancer of the pharynx, and so forth. Both in men and women there is a very intimate connection between the whole region of the upper respiratory tract, the nose, pharynx, and larynx, and the sexual organs; and many of the more obscure neuroses of these regions have a sexual basis. That such a special if somewhat mysterious connection exists, has long been known. Its physiological correlation in man is found in the sudden development of the larynx during the time of puberty, particularly in men, accompanied by characteristic changes in the voice, known as the "break of the voice"; whilst in the woman a slight huskiness of the voice and other indefinite phenomena are often noticeable at the time of menstruation; practised singers often notice the deteriorating influence of the menstrual period on the voice. The effect of castration of boys in modifying these changes in the larynx is well known. In the lower animals this physiological connection is seen, again, in the "roaring" of the otherwise silent stag at the rutting time; while numerous well-authenticated cases of vicarious bleeding from the nose or pharynx, replacing the menstrual flow more or less completely, have been recorded.

While the influence of the sexual organs on the respiratory organs is most obviously recognised in the larynx by the alterations in the voice, many of the purely subjective neuroses are referred indefinitely to the throat region generally. As Schadewaldt pointed out, the power of localising sensations felt in the throat is very defective physiologically as well as pathologically; "the sensations in the most different parts of the organs of the neck are, as a rule, jointly referred to a region in which, so to speak, the joint sphere of sensation (the sensorium commune, according to analogy) of the entire throat is situated." This region is the front part of the neck, the "laryngo-tracheal region" (Gottstein). It is therefore of no use to attempt to distinguish the subjective sensory neuroses of the pharynx from the rest of the upper respiratory tract, as an attempt of this kind might easily lead to therapeutic mistakes.

Chlorotic and anæmic girls, and women at the climacteric period, very frequently suffer from paræsthesia of the throat region; but it is the latter class who afford the great majority of instances and in the aggravated forms. The "sensory throat neuroses of the climacteric period," as they have been called by one of us (F. S.), may be classed under two headings, "paræsthesia" and "neuralgia" cases, the former class being the more frequent. We have never seen a case of anæsthesia of the throat due to the climacteric period. The majority of cases of climacteric throat neuroses occur in women who are by no means of a neurotic or hysterical type. Most frequently patients complain of unpleasant sensations which often enough cannot be described exactly; in some cases they are general, in others they shift from one part to the other. In other cases, again, the patients speak of general or partial "soreness," "dryness," "tickling," of a desire to be constantly "scraping," or "hawking" and "hemming," of sensations of "choking" or "strangulation," or of a feeling as if the throat were "wooden"; very frequently there is a sensation as of a foreign body, variously compared to a crumb of bread, a bone, a hair, or a needle, or a constant desire to "swallow empty," or feelings of heat or cold. But in very many cases one sees how the patients strive in vain to describe exactly what they feel, and to define the seat of the sensation. Much less frequently there are "neuralgic" sensations, described as a fixed pain on one side of the throat, sometimes radiating to the ear and temporarily diminished by swallowing.

The intensity of these neuroses varies most remarkably; in some, the sensations are merely felt as an inconvenience; in others, the subjective troubles are of a more severe kind. The patients not rarely even cry whilst relating the history of their ailment; and the general depression accompanying the affection is sometimes so great that in a good many cases the patient dreads cancer, consumption, syphilis, or some other organic disease of the throat.

The throat symptoms complained of may be the only sign of the approaching change of life; or sometimes may even precede the menstrual irregularities; in other cases they follow the usual uterine disturbances of the climacteric period, or are associated with dyspepsia, insomnia, and other complications commonly observed at the menopause.

Objectively there may be little or absolutely nothing to be seen in the throat. In some cases a few small pharyngeal granulations, or a slight enlargement of the lingual tonsil, or some hardly noticeable thickening of the lateral folds of the pharynx, are detected. It is important to guard against two sources of error; namely, of overlooking some actual and tangible cause of the affection, or, on the other hand, of wrongfully attributing the neuroses to any slight abnormality. The objective symptoms in the cases which belong to the domain of paræsthesia and hyperæsthesia, and of the sensory neuroses of the climacteric period, are either conspicuous by their absence, or the changes found are so slight as to make it extremely unlikely that they can be held responsible for the subjective phenomena. On the other hand, it ought to be remembered that paræsthesia, hyperæsthesia, or neuralgia of the throat may be the first sign of malignant disease of the part or of its neighbourhood; and that the age at which the climacteric neuroses come under observation is identical with that in which the beginning of malignant mischief is most frequently observed. Before arriving at a diagnosis of sensory throat neuroses, we must first, by careful examination, exclude chronic pharyngeal catarrh in its definite forms, considerable nasal stenosis, a foreign body, considerable enlargement of the lymphatic tissue at the base of the tongue, general anæmia of the pharynx—particularly in cases of commencing tuberculous disease of the lungs, and general neurasthenia or hypochondriasis.

The *treatment* of sensory neuroses will of course depend on the cause. In bulbar paralysis and other central organic nervous affections treatment is practically useless; while in post-diphtheritic anæsthesia the treatment is the same as that indicated in the motor paralysis with which it is almost invariably associated; namely, gentle faradism or galvanism combined with hypodermic injections of strychnine. As regards hyperæsthesia and anæsthesia, the treatment must be directed to improve the general health and to remove any possible local cause; and in cases in which there is any reasonable doubt whether the neuroses be due to the climacteric period or to some local mischief, the latter should always be treated, while at the same time our suspicions that the affection depends upon the "change of life" ought to lead us to feel that if the local therapy fails to give relief the patient should not be discouraged, but should be induced to look forward with confidence to its spontaneous disappearance in course of time. In cases of neuralgia particularly the probe ought to be used in order to ascertain whether there be any tender spot in the painful part; anæmia and chlorosis should be treated by the cautious use of iron and arsenic. The usual local remedies—astringents and caustics—are generally quite useless, or have but a very transitory effect; and their indiscriminate use is to be strongly condemned, inasmuch as this whole period of a woman's life is in itself associated often enough with a state of mental depression: thus, after the failure of local means, patients are prone to become still more depressed and more than ever convinced that their ailment is really of a serious nature. This caution applies particularly to the use of narcotics, such as opium, cocaine, bromide of potassium, and the like, which, whether locally or constitutionally employed, after a very short time lose their effects, and the patients either become enslaved by a pernicious habit, or by abstinence from the accustomed drugs their general and local sufferings are considerably increased. In severe cases of paræsthesia, and more particularly in cases of neuralgia, we should use those drugs only which cannot do any possible harm, such as menthol in spray and general tonics. The best effects are certainly obtained in those climacteric cases in which the throat neurosis is associated with considerable increase in bulk, digestive disturbances, and gouty manifestations. In such cases, if the patients can be persuaded to go through a mild course of the mineral waters of Carlsbad, Marienbad, Kissingen, Aix-les-Bains, or Vichy, a disappearance of all the symptoms complained of and a restoration of balance are often much sooner obtained than in ordinary forms of climacteric neurosis. But in the great majority of cases no treatment other than moral influence is either necessary or desirable.

Foreign bodies in the air and upper food passages.—It is convenient that the subject of foreign bodies in the fauces, pharynx, larynx, and trachea should be considered together for two reasons: first, on account of the very important fact that the power of localisation of sensations felt in the throat is extremely defective, and sensations arising in any part of this region are generally subjectively referred to one common region, namely, to the front part of the neck corresponding to the larynx and upper part of the trachea, the *laryngo-tracheal region*; and, secondly, because the invading body is obviously liable at any moment to pass from one region to another, with or without modification in the symptoms presented. These remarks do not apply to the same extent to the nasal passages proper [*vide* p. 701].

It is unnecessary to enumerate the various foreign bodies that may become impacted in the throat; our purpose is mainly to consider the chief difficulties that may be encountered in the diagnosis, and the principles that should guide us in the treatment of these cases.

In a considerable proportion of the patients who present themselves for the removal of foreign bodies in the throat, the foreign body has already been dislodged, and it is the persistent sensation only which leads the patient still to believe that it is actually there. These after-sensations of pain, pricking, and soreness, or of the actual presence of the foreign body, are apparently far more lasting in this region than is the case in other sensitive parts, such as the eye; and it is important to remember that in spite of the most positive assurances, even of educated persons, that the foreign body is still present, it may long have passed down, leaving behind, however, strangely vivid and persistent after-sensations: more especially is this the case when foreign bodies have been impacted in the pharynx, tonsils, and the upper part of the œsophagus. On the other hand, we cannot too strongly insist on the necessity for a most thorough and methodical examination of all the parts in question; and only after a positive exclusion of the possibility of the continued presence of the foreign body are we warranted in arriving at a diagnosis of a persistent after-sensation only, and in telling the patient that the foreign body is no longer impacted.

In all cases except those of immediate urgency (see farther on under the head of "Treatment") the examination should be begun by inspection, and not by digital exploration. Palpation may be desirable or necessary when inspection has failed; but it is always attended with the risk of dislodging the foreign body and driving it farther down, possibly into the lower air-passages; while in the case of small pointed bodies, such as fine fish-bones, pins, and needles, which are already deeply buried in the tissues, the still projecting portion may be pushed in still farther and completely buried, whereby subsequent attempts at removal are made more difficult if not altogether frustrated. For the same reason, if cocaine is to be used to diminish the soreness and irritability of the parts, it should be applied by means of a spray, and not by a brush, which is open to the risk of producing the same undesirable result as digital exploration. For the inspection of the throat a good light is essential, and the examination should extend to every region in turn, and not be limited to an inspection of the one part which the patient indicates as being in his opinion the place where the foreign body is lodged; inasmuch as the subjective sensation of localisation is very deceptive. This fact is well illustrated by the personal experience of one of us (F. S.), in whom the sensations caused by a piece of partridge bone impacted in the throat were felt at a distance of at least two or three inches from the spot where it was really impacted. A patient may positively state, as he did in his own case, that he felt sure the foreign body was impacted in the region of the larynx, whereas in reality it had stuck in the posterior wall of the pharynx behind the uvula. This instance well exemplifies the necessity for a really methodical examination; and an observer who trusts the patient's statements in these cases, and only examines the laryngeal region, neglecting a thorough inspection of the fauces and naso-pharynx, may have the mortification of hearing afterwards that another physician had actually removed the foreign body from a part unsuspected.

It is advisable, therefore, to begin the examination with inspection of the fauces, particularly noting that the foreign body is not lying concealed by the anterior pillars of the fauces or by the tonsils. Next we should observe the glosso-epiglottic fossæ and lingual tonsils, before thoroughly examining every part of the larynx and the upper end of the œsophagus with the laryngoscope; finally, the rhino-pharynx should be explored. Particular care should be taken when the foreign body is a fish-bone; for, if so deeply impacted in the tissues that only a small part projects, it is sometimes extremely difficult to discover it; the more so as strings of tenacious saliva extending from one part of the throat to another often closely simulate it. In such cases examination with the probe, under the guidance of a good light and, if necessary, of the laryngoscope, ought to establish the actual existence of the supposed body in the tissues before an attempt is made to introduce forceps or other instruments for removal.

Quite recently our means of detecting foreign bodies in the upper air and food passages, those at any rate which are impenetrable to the Röntgen X rays, have been enriched by the introduction of that method of examination; and there can be no doubt that it will prove of the highest value in cases in which coins, buttons, needles, bones, and similar foreign bodies impenetrable to light have become impacted in these parts and cannot be discovered by the ordinary methods.

It is impossible to form any definite classification of the foreign bodies that may be encountered in the different regions; but speaking generally, it may be said, as a rule, that only sharp-pointed bodies—such as pins, needles, and small pointed pieces of meat or game bones and fish-bones—become fixed in the fauces and rhino-pharynx, though they are equally apt to be caught in the larynx or œsophagus. Coins and small rounded bodies usually pass down till they are impacted in the larynx, œsophagus, or lower air-passages. In the larynx they are most apt to lodge in the pyriform sinuses, or to lie across the glottic opening, upon the ventricular bands, or between the ventricles of Morgagni.

Owing to the funnel-shaped narrowing of the lower end of the pharynx, and to the fact that the narrowest part is at the level of the cricoid cartilage, foreign bodies, if arrested on their passage downwards, are particularly apt to lodge at this spot. Bodies which pass into the bronchi most frequently lie on the bifurcation, or pass into the right bronchus; the right bronchus being the seat of lodgment about twice as frequently as the left.

Symptoms.—While the primary symptoms of a foreign body in the throat, and particularly in the larynx, are generally sufficiently obvious when the patient states the cause of his suffering, it is important to bear in mind that some cases of apparently sudden loss of consciousness may be due to occlusion of the glottis by a foreign body; and if summoned to a case where the patient is said to have had a fit or to have become suddenly unconscious whilst eating, the possibility of such an accident should not be forgotten.

In children especially, foreign bodies are liable to be swallowed or drawn into the air-passages unconsciously, where they may set up more or less acute dyspnœa or obstruction to deglutition. One of us (W. W.) recently saw a case which presented all the symptoms of croupous laryngitis, and, dyspnœa becoming urgent, tracheotomy had been performed. The symptoms abruptly subsided when a piece of nut-shell was coughed up and revealed the true character of the complaint, after it had been arrested for six days. This case well illustrates the necessity of thinking of foreign bodies when an obscure inflammatory affection or a swelling is seen in the air or food passages, even though no history of the impaction be obtainable. These remarks apply with no less force to the cases of adult patients.

Hæmorrhage may result from direct injury by a sharp body; thus Mr. Rivington records a case in which a fish-bone, which had lodged in the pharynx, penetrated the common carotid and necessitated ligature of the artery. The puncture was believed by Rivington to be due to the use of a probang whereby the fish-bone was pushed through the wall of the pharynx.

If a foreign body has lodged between the vocal cords, and, owing to the small size or peculiar position or shape of the invading body, acute asphyxia is not induced, aphonia may be the most notable symptom; and when it passes into the trachea or a bronchus, violent coughing and dyspnœa will be experienced. On the other hand, especially after the initial symptoms have passed off—such as pain, or coughing and dyspnœa, if the body lodge in the larynx, or the sensation of the presence of a foreign body if it lodge elsewhere,—there may be no indication whatever of its presence; nevertheless a careful exploration of the whole region should be made, as secondary mischief may subsequently arise.

Very frequently foreign bodies, which shortly after their impaction cause slight symptoms or none at all, may later be the source of most serious troubles. Secondary symptoms are generally of the nature of inflammation or ulceration, in consequence of which an abscess may form and the pus may burrow in the structures, or even set up suppuration in the mediastinum. In the larynx a foreign body, after originally giving but little trouble, may cause subsequent perichondritis and lasting disablement of the organ; or, after having remained in the larynx for some time, may become dislodged and fall into the lower air-passages, setting up most serious disease there. If a bronchus have been invaded, secondary pneumonia and pulmonary abscess or bronchiectasis are apt to supervene. Sometimes penetration of the structures in the neck causes extensive subcutaneous emphysema. In the œsophagus after a while it may either perforate the wall or lead to the formation of a pouch. Copper coins may give rise to metallic poisoning; and foreign bodies more or less occluding the œsophagus may produce such a degree of dysphagia as seriously to interfere with deglutition and nutrition.

All these contingencies are so grave that we cannot contemplate the impaction of a foreign body in these parts with indifference, even if at first it be unattended by serious symptoms.

Treatment.—We have already spoken of the necessity of methodical investigation preceding any therapeutical effort in ordinary cases. When, however, the lodgment of a foreign body in the air-passages results in dyspnœa so urgent as to threaten immediate asphyxia, or has actually caused loss of consciousness, there is obviously no time for a careful examination of the throat; the forefinger should be cautiously passed at once down to the larynx, and, if the cause of the obstruction can be felt, the body may be dislodged; but it is important to avoid pushing the foreign body into the trachea. If nothing can be felt in the larynx, and the urgency of the case permit, the patient should be inverted. In this position a sharp blow on the back may dislodge the foreign body from the trachea or bronchus, and cause it to fall into the larynx, whence, possibly by inducing coughing, it may be expelled without tracheotomy. But should our efforts prove futile, tracheotomy should be performed promptly; and if, nevertheless, dyspnœa be still urgent the patient should again be inverted, and every effort made to cause the foreign body to pass into the upper region of the trachea, whence it may be extracted through the tracheotomy wound.

In the vast majority of patients who seek medical aid complaining of a foreign body in the larynx, the symptoms are less urgent; or, if at first alarming, the acuter manifestations of the presence of the impacted body have subsided; under these circumstances both the examination and the treatment can be carefully and methodically conducted.

Two principles ought to guide the practitioner in treating these cases:—

First, no foreign body, the presence of which has actually been detected, should be permitted to remain impacted, even although at the time it may not produce any active symptoms; we have already pointed out the very serious secondary symptoms which may arise nevertheless. In the face of these risks it is hardly necessary to emphasise the importance of leaving no justifiable means of removing the foreign body untried.

Secondly, no attempt should ever be made forcibly to ram down an angular or pointed foreign body. The danger of passing bougies or probangs for this purpose is self-evident; yet this risk is very frequently ignored, and consequently perforation of the carotid or the descending aorta, tearing or perforation of the pharyngeal and œsophageal walls, and many other such serious results, have actually occurred.

Needless to say, no definite rules can be laid down for the best method of removing the various foreign bodies that may become impacted in the regions in question; the practitioner must be guided in each case by (*a*) the nature and size of the foreign body, and (*b*) the spot in which it has become lodged. In cases of impaction of foreign bodies in the pharynx and rhino-pharyngeal cavity, forceps with indented blades will in most instances be the most suitable instrument, the curve of the forceps being adapted to the locality of the impaction.

When the body has passed down into the larynx, or into the lower air-passages, and when its form is round or circular, as of coins, beans, peas, and so forth, it is always worth while, before any instrumental interference, to try inversion and forcible shaking of the patient; the plan may even be adopted when the foreign body is pointed or angular. In a most remarkable case, seen by one of us (F. S.) and described by Mr. Pitts, an earring, which had first become impacted in the larynx just below the vocal cord, and a few days afterwards had fallen into the left bronchus, was spontaneously evacuated by coughing about an hour after inversion and shaking had been tried, apparently without success.

Should the foreign body be fixed in the larynx itself, and should its nature be such as to allow of the hope of removing it by intra-laryngeal operation without injury, this plan of treatment will, of course, be preferable to an external incision. Should it be too large, however, or too irregular to justify such attempts, and should it moreover cause dyspnœa, tracheotomy might first be performed, and an attempt be made to get hold of it through the tracheotomy wound, or to dislodge it from the larynx into the pharynx, where it can, of course, be grasped more easily; or, if this should fail, tracheotomy may be carried forward to thyrotomy and the foreign body thus removed.

A similar plan of treatment is called for when foreign bodies of large size and angular shape have lodged in the trachea; and in cases in which the foreign body is situated in one of the bronchi, tracheotomy, followed by an attempt at extraction by means of very long slender forceps, is advisable. If the foreign body cannot be extracted at the time of the operation itself, it will be desirable not to insert a tracheotomy tube, but to keep the tracheal wound open by stitches in the trachea attached to an elastic band carried from the two sides of the wound round the neck posteriorly; thus, in the event of the foreign body becoming subsequently dislodged, it can easily be expectorated through the open wound during the act of coughing. When bodies are impacted in the œsophagus, a parasol probang may be cautiously passed down and withdrawn opened, so as possibly to catch the body in its meshes. In some cases the coin-catcher is required. Only when it is quite certain that the offending substance is of a soft or rounded form can it be justifiable to push it down into the stomach.

Of course extraordinary cases require special measures; the necessity of œsophagotomy or gastrotomy may even arise: but the problems of dealing with these various cases and the mode of treatment to be adopted are of a purely surgical kind, and beyond the scope of the present article.

Diseases of the Tonsils.—*Introductory remarks.*—We have no certain knowledge of the physiological functions of the faucial, lingual, and pharyngeal tonsils; but Philip Stoehr has drawn attention to the fact that in their epithelial covering are gaps large enough to allow the passage of leucocytes; an enormous transit of such cells undoubtedly occurs into the tonsils without actual destruction of the epithelial strands. The leucocytes or phagocytes are protective against the invasion of the pathogenetic microbes which are brought into the fauces and naso-pharynx by inspiration; although it may well be that they have other unrecognised functions also to fulfil. However this may be, whilst the fissures and crypts of the tonsil form convenient resting-places or "traps" for microbes, the peculiar anatomical arrangement of their epithelial covering opens the gates to their invasion; and thus it is easy to understand how the tonsils, especially if the vitality and resisting power of the tissues be flagging, may form a portal for the invasion of the system by pathogenetic organisms. Recent researches furnish abundant proof of the correctness of these surmises. In addition to the demonstration of tubercle and other bacilli in the tonsils by Buschke, Schlenker, Krueckmann, Strassmann and Dmochowski, Dieulafoy and Cornil have found that of seventy adenoid tumours examined microscopically, four (that is, one in seventeen) showed unmistakable evidence of tuberculous giant cells. As the result of an investigation into the part of the tonsil in scarlatinal infection, Walter Dowson was led to the conclusion that the tonsiliar lesion and cervical bubo of scarlet fever are the analogues of the chancre and bubo of syphilis. That diphtheria preferentially makes its first appearance on the tonsils is well known, and in a series of cases of septic inflammation of the throat and neck recently published by one of us (F. S.), acute tonsillitis formed one of the initial symptoms in a considerable proportion; while the researches of Sendziak and others have proved that acute lacunar tonsillitis is due to direct infection by streptococci, staphylococci, and pseudo-diphtheritic bacilli. Finally, Suchannek has recently summarised the previous observations on the connection of rheumatism with tonsillar affections, and has rendered it highly probable that in many cases the specific poison of rheumatic fever also obtains its entrance into the organism through the portal of the tonsils.

In view of such facts as these, it is obvious that the tonsils play a very much more important part in admitting the various infecting microbes than has hitherto been conceded; and we have no doubt that their condition merits close attention when the question of the etiology of infectious diseases is discussed.

Acute Tonsillitis.—We distinguish three clinical forms:—(i.) *Superficial or lacunar tonsillitis*, with diffuse inflammation of the mucous membrane of the tonsil and accumulation in the crypts of a great number of bacteria (small diplococci especially), and of lymphoid corpuscles contained in a fibrinous network and appearing in the mouths of the distended crypts as discrete patches of yellowish exudation. While this exudation is mainly lying on the surface of the epithelium, small necrotic points have been observed where the process has extended into the superficial layers of tissue (Sokolowski and Dmochowski). (ii.) *Parenchymatous tonsillitis*, in which the deeper tissues of the body of the tonsil are mainly inflamed, the amount of swelling being considerable. (iii.) *Peritonsillitis*, in which the connective tissues in front of the tonsil are chiefly involved.

Suppuration is especially prone to follow peritonsillitis, but lacunar and parenchymatous tonsillitis may also end in suppuration.

Acute lacunar tonsillitis is undoubtedly an infectious disease, which is associated with various micro-organisms, and may be induced by a variety of causes. It is especially prevalent in the late autumn and early spring, and is frequently epidemic; and numerous instances have occurred in which the affection has run through a household, affecting its various members in turn. Overwork, anxiety, and all causes, whether local or general, which lower the resisting power of the tissues, render the individual more liable to infection. Thus chronic hypertrophy and degeneration of the tonsils indirectly dispose to attacks. In many cases attacks of arthritic rheumatism directly precede or follow the tonsillitis; and, indeed, the causes of rheumatism, such as exposure to cold and damp, or to sudden changes in temperature, are likewise important causes of tonsillitis. Tonsillitis is commonly one of the initial symptoms in measles and scarlet fever, and is often met with in diphtheria and secondary syphilis. In not a few cases tonsillitis is due to septic poisoning; and the frequent occurrence of attacks of tonsillitis in a household, like all forms of recurrent sore throat, should lead us to suspect bad drainage. Again, it may occur traumatically, as by injury by a spicule of bone in the food, or by mechanical injury; and it is sometimes set up by the presence of calcareous cheesy masses in the crypts.

Tonsillitis is essentially a disease of early adolescence, but may occur at any time of life from earliest infancy to extreme old age.

The symptoms vary very much in degree in different cases. The attack generally begins with soreness and stiffness in the throat for one day, with aching in the back and limbs, headache and general feeling of malaise, followed by a rigor with sudden rise of temperature which soon reaches 104° to 105° F.; the pulse is frequent, full, and bounding. With the onset of swelling and inflammation of the tonsils, pain darting up to the ears, and dysphagia, are prominent symptoms, and are often agonising. The constant desire to swallow is dreaded because of the pain of it; the accumulating saliva therefore dribbles from the mouth. The tongue becomes thickly coated, and the bowels constipated. The urine is scanty, high-coloured, rich in urea and urates, and sometimes contains albumin. The spleen is often enlarged. The mouth can scarcely be opened, partly on account of the swelling of the tonsils, and often of the submaxillary tenderness and tumefaction also. Catarrhal inflammation always extends more or less from the tonsils to the fauces and pharynx. The rhino-pharyngeal tonsil is likewise involved with much greater frequency than is generally believed; and this must very often be held to account for the deafness and tinnitus due to stoppage of the Eustachian tubes. The lingual tonsil is also liable to attack; Sendziak observed this complication in twelve patients out of 133 cases of lacunar tonsillitis. When suppuration has begun, the pain and tenderness are greatly increased. In suppurative peritonsillitis, though the pain is more pronounced than in the first two clinical varieties, the general disturbance and febrile symptoms are often slighter. In the lacunar and parenchymatous forms both tonsils generally become involved, though as a rule one tonsil is affected earlier or to a greater degree than the other: peritonsillitis is almost always unilateral.

The course of the affection is rapid, seldom lasting more than two days or a week, and ending in resolution or suppuration; but the subsequent prostration may be extreme.

Diagnosis.—In peritonsillitis the tonsil is often slightly inflamed or not at all—a redness and smooth forward bulging may be observed on one side of the soft palate; in parenchymatous and lacunar tonsillitis the tonsils themselves are always red and swollen. In the latter form the discrete patches of yellowish exudation from the crypts are ordinarily characteristic enough to prevent confusion with diphtheria; but in not a few cases a differential diagnosis is impossible without resorting to bacterial cultures, for the lacunar exudations may spread beyond the crypts, and, becoming confluent, may form a sort of false membrane sometimes adherent to the tissues and indistinguishable from a diphtheritic membrane. The points in favour of diphtheria are (*a*) a false membrane of a grayish white colour, thick and firmly adherent, and involving the pillars of the fauces, the soft palate, or uvula; (*b*) the early presence of albumin in the urine in considerable amount, with a low or only slightly raised temperature, little pain, and unilateral affection. Submaxillary swelling and enlarged cervical lymphatic glands are common to diphtheria and tonsillitis.

We must further remember that, instead of the usual tough, gray, adherent false membrane, diphtheria may be associated with a soft, pultaceous exudation which may be restricted to the crypts, or may occur with no visible false membrane. In these doubtful cases it will always be advisable to leave the diagnosis in suspense for twenty-four hours until cultures have been made.

Prognosis.—In simple tonsillitis the prognosis is nearly always favourable; but we must be on our guard lest we overlook the earlier manifestation of the more virulent septic forms, which may result in œdematous, erysipelatous, or phlegmonous laryngitis, or in purulent cervical cellulitis (angina Ludovici), spreading to the mediastinal glands; or in general infection with resulting endocarditis or pericarditis, infective phlebitis, orchitis, or ovaritis. Further, tonsillitis may be the precursor of an attack of acute rheumatism, or less frequently of acute gout. Very rarely paralytic sequels have occurred; and though no doubt palsies of the soft palate, ocular muscles, or other parts are strong presumptive evidence of the diphtheritic nature of the case, yet in a few of these careful investigation has failed to reveal the Klebs-Löffler bacillus. Cases of death from suffocation in young children by excessively swollen tonsils are recorded; and it has been necessary to perform tracheotomy to prevent asphyxia from laryngitis consequent on the tonsillitis. Death has occurred from rupture of tonsillar abscess and escape of pus into the larynx.

Treatment.—From the outset the bowels should be kept freely moved, preferably by saline aperients. If the temperature be much above the normal, six grains of sulphate of quinine should be given every four hours till it is reduced. In rheumatic cases, where there is much aching pain in the limbs and back, tincture of guaiacum, or fifteen to twenty grains of salicylic acid, or the soda salt, given every two hours, will often alleviate the symptoms. Tincture of aconite in small and frequently repeated doses is useful in young children. In parenchymatous tonsillitis, especially, guaiacum lozenges should be prescribed, six to eight being slowly dissolved in the mouth in the twenty-four hours. Gargling with dilute solutions of chlorate or permanganate of potash to which phenazonum, ten or fifteen grains to the ounce, has been added, is most useful; and sucking ice often gives considerable relief. But if the pain and swelling are considerable, gargling may be out of the question; then hot fomentations applied to the neck and lower angle of the jaw, or a spray of cocaine (2 to 5 per cent) or of menthol (10 to 15 per cent) dissolved in colourless oil of vaseline or in oleum adepsin, will lessen the pain. The two solutions may be combined; for menthol has the additional advantage of being antiseptic. Firm compression with the tips of the fingers applied just in front of the external auditory meatus will greatly relieve the pain on swallowing. In some cases a few longitudinal incisions in the tonsils will relieve congestion and pain. Any indication of suppuration should be watched for, especially in peritonsillitis; in such cases the inhalation of steam or gargling with warm water relieves the pain and tends to make the pus point. In cases of peritonsillitis, when the soft palate is seen to be bulging forwards and fluctuation is felt through it, the incision always ought to be made—not, as many practitioners still do, behind the palate into the substance of the tonsil itself, but through the palate in the direction from without and below, inwards and upwards.

The tonsils, as a rule, should not be removed while inflamed: to this rule, however, two exceptions may be given; namely, when in children respiration is greatly embarrassed by the tonsillar swelling, and when in adults tonsillitis has repeatedly occurred, but removal during the period of quiescence is for one reason or another impossible.

Patients are generally much weakened by tonsillitis, and need feeding up, and suitable tonics such as iron and quinine.

As tonsillitis, or at any rate the acute lacunar form of it, is certainly infectious, it is well to advise the patient's friends to avoid such immediate contact as kissing; children and persons specially prone to the affection should keep away, but strict isolation is not so necessary as in the case of diphtheria.

Chronic Enlargement of the Tonsil.—*Causes.*—Hypertrophy of the tonsils is one of the affections in which the influence of heredity is most obviously seen, particularly in families in which other evidences of "scrofula" or of the "strumous" diathesis exist. Various exanthems, measles, for instance, scarlet fever, and diphtheria, strongly dispose to it, while in many cases it results from repeated attacks of tonsillitis. The enlargement may date from infancy or occur at puberty. Large hypertrophy is rare after thirty-five; and the tonsils, if enlarged in childhood, tend to atrophy at puberty: although it is important to know that this rule is by no means without exception. In many cases there is no obvious cause for the condition; but in most there is a combination of several of the above contributory factors. Very frequently it is found associated with hypertrophy of the pharyngeal tonsil (adenoid vegetations), and, not quite so often, with enlargement of the lingual tonsil and of the cervical lymphatic glands.

Pathology.—The substance of the healthy tonsil is composed of a number of small nodules of lymphatic tissue arranged around a group of seven to twelve crypts, and of connective tissue, blood-vessels and a few nerve fibres; the tonsils are covered by ordinary mucous membrane which dips down into the crypts. There are no secretory ducts, nor does the mucous membrane even in the crypts present any appearance of muciparous glands; but leucocytes pass out through minute spaces between the epithelial cells, and the mucous membrane is capable of secreting small quantities of mucus. In the large soft chronic hypertrophy of the tonsils, such as is generally seen in young patients, the lymphatic tissue nodules are increased in size and number, and the gaping crypts contain a variable amount of mucus and of altered epithelium undergoing fatty degeneration. In other cases, chiefly in adults, the hypertrophy is mainly due to an excessive growth of the connective tissue elements, which, by compression, cause more or less atrophy of the lymphatic nodules and blood-vessels, and obliteration of the crypts; changes which result in a hard, smooth, non-vascular tonsil.

We distinguish three clinical varieties:—(i.) *Chronic lacunar tonsillitis* with accumulation of caseous matter in the crypts, which gape when the yellow evil-smelling masses are extruded. These masses are sometimes very consistent, and may be confused with pharyngomycosis leptothricia; but examination of the very adherent, clear, milky-white, opaque, soft, projecting pointed masses of the latter will reveal the characteristic threads of the cryptogam. (ii.) *Chronic parenchymatous hyperplasia.* The tonsils are soft and friable from the overgrowth of lymphoid tissue. (iii.) *Chronic fibroid degeneration.* This form is almost confined to adults, it represents the advanced stage of the hyperplastic form, it is often the remnant of former frequently occurring attacks of acute tonsillitis, and it is especially associated with the rheumatic or gouty habit.

Sometimes we meet with a smooth, pale yellowish swelling due to occlusion of the mouth of a crypt with retention of the cheesy exudation —a form of chronic tonsillar abscess.

The enlargement of the tonsils is sometimes very great, occasionally enormous, projecting far beyond the palatine arches, and meeting in the middle line behind the uvula. Not infrequently the anterior pillar of the fauces has become adherent to the tonsils, and extends over the whole anterior surface, completely concealing the tonsil itself.

Symptoms.—Owing to the enlarged tonsils encroaching on the oro-pharyngeal space, and interfering with the movements of the soft palate, the voice is throaty and thick, with a nasal twang. Pain is generally absent, except in subacute attacks of tonsillitis, which generally occur at frequent intervals. In children especially, in whom most of the cases are met with, post-nasal adenoids are generally present also, and many of the symptoms attributed to enlarged tonsils—such as anæmia, buccal respiration, pigeon breast, and infra-mammary depression of the ribs, small ill-developed lungs, snoring, suffocative symptoms, and night-terrors during sleep, difficulty in deglutition, and particularly Eustachian deafness—are in the main due to the concomitant adenoids; though most of these symptoms may be due to the tonsillar disease alone, without adenoids. The mouth is often kept open, the under lip protruding; and thickening behind the angle of the jaw and enlargement of the cervical lymphatic glands are frequently present. Dry reflex cough is a very common symptom, and various reflex neuroses, such as darting pains in the ears, vomiting and gastric pains have been attributed to enlarged tonsils. The constantly recurring attacks of tonsillitis, in addition to the suffering they entail, are attended by high fever and followed by great prostration; thus they greatly interfere with occupation, development, and general health.

Chronic enlargement of the tonsils may then act injuriously in three different ways—namely, (*a*) by mechanically obstructing the food and air passages; (*b*) by maintaining a liability to frequent, often very painful attacks of inflammation within the glands themselves or in their immediate neighbourhood; (*c*) by forming a perpetual source of danger from infection by various micro-organisms, such as those of diphtheria or tubercle.

The prognosis, as regards the life of the patient, is invariably good; the ultimate effect on the health of the patient will depend to a certain extent on his age, on the relative degree of hypertrophy of the tonsils as compared with the size of the fauces, and on the presence or absence of concomitant adenoid vegetations in the rhino-pharynx.

In children under the age of ten marked hypertrophy greatly interferes with growth and healthy development; and the coexistence of adenoids adds to the pernicious effects that will almost certainly ensue to his permanent disadvantage. A tonsil not excessively hypertrophied may undergo the physiological retrogressive changes soon after the age of puberty; but in most cases we shall await such a happy consummation in vain, and meanwhile the child is exposed to the many risks which we have already described.

From a therapeutic standpoint the prognosis is excellent provided no irremediable consequences have ensued; thus the prospect of perfect recovery depends on the absence of marked deformity of the chest walls and other secondary changes.

Treatment.—The only satisfactory method of dealing with enlarged tonsils which require treatment is to remove them; and at the outset we would emphasise the uselessness of the so-called milder measures, particularly the ridiculous painting with iodine solutions, tannic acid, and the like: these prescriptions are so much waste of time, and generally succeed only in causing considerable annoyance to the patient.

The tonsils should be reduced in size, (*a*) if they interfere with respiration, either during waking or sleep, and lead to deficient aeration of the blood; (*b*) if they lead to changes in the character of the voice and to defective articulation; (*c*) if they lead to defective development of the face and chest; (*d*) if the chronic enlargement, though not very considerable, be attended with frequent attacks of inflammation of the tonsils themselves, by tumefactions of the cervical glands, or by catarrhal conditions of the neighbouring mucous membranes, especially of the Eustachian tubes: even in the absence of symptoms, decided chronic hypertrophy, especially in association with the strumous diathesis, renders an operation advisable in patients under fourteen, so that a very active source of danger from infection may be removed.

Removal of the tonsils may be accomplished by various methods: by cutting with the bistoury or tonsillotome, by enucleation, or by the galvano-caustic point or snare. Our practice is confined to two methods, namely, tonsillotomy and the galvano-caustic point. When it has been decided to remove the tonsils we have to consider which is the best method to choose. (*a*) If the patient be under twenty, and the enlargement be mainly transverse, so that the tonsil or tonsils project a good deal beyond the arch of the palate, the cutting operation should be preferred. (*β*) Local conditions being the same, but the patient over twenty years of age, and in all cases where the tonsils are entirely concealed behind the palatine arches, or only project a little beyond them, let broad applications of the galvano-cautery be made by means of a large flat burner of platinum or porcelain. The tonsils are reduced in size by the cautery quite as rapidly and effectually by this method as by galvano-puncture; and it has the advantage of greatly reducing the risk of sharp hæmorrhage, a risk which cannot altogether be disregarded. The cutting operation in patients over twenty is more liable to be attended with serious and uncontrollable hæmorrhage than is the case in younger patients.

The object of the operation should be to reduce the tonsil to the normal size; and therefore in using the tonsillotome it is well at the moment of performing the operation to push the tonsil a little inwards by firm pressure from without just underneath the angle of the jaw, so that the portion of the tonsil lying between the palatine arches is removed without either injuring the anterior arch of the palate or running a risk of injury to the large vessels in close relation with the base of the tonsil. It is idle to remove a superficial slice in the hope that the remainder will atrophy.

When the galvano-cautery is employed, the reduction of the tonsils will require six, eight, or ten sittings, according to the degree of enlargement, at intervals of three days to a week. The amount of reduction will have to be determined on the merits of each case.

Removal is most readily accomplished by the tonsillotome. We employ Mackenzie's instrument, though by one of us (W. W.) Reiner's modification is often preferred. In young and nervous children the operation may be done under chloroform administered as in operating on post-nasal adenoids. Again we wish to emphasise the rule that in all cases of enlargement of the tonsils adenoids should be sought; and, if present, they should be removed first. In adults and in older children, when the tonsils only require removal, a general anæsthetic may be dispensed with, and a strong solution of cocaine or eucaine used instead to produce local anæsthesia. After operation the patient should be directed to keep quiet for a few days, and only bland, cold, and soft food should be taken.

Hæmorrhage is always pretty free after tonsillotomy, but usually ceases spontaneously in a few minutes. Dangerous hæmorrhage occurs in a very small percentage of cases, however skilfully the operation is performed; yet so rarely in proportion to the number of operations, that it can never be urged as a general objection to the practice. In children it is extremely rare; and it is in the older patients whose enlarged tonsils have undergone cicatricial degeneration that hæmorrhage is to be feared, and this more especially after cutting operations.

The causes of hæmorrhage may be stated briefly as (*a*) abnormality in the distribution of the blood-vessels; (*b*) fibroid tissue deposit and degeneration of the walls of the vessels, which gape when they are divided; (*c*) hæmophilia; (*d*) eating solid food, and (*e*) over-use of the voice too soon after the operation.

If the hæmorrhage do not soon cease spontaneously, or if secondary hæmorrhage occur, the patient should be kept quiet and have small pieces of ice to suck, and a mixture of tannic and gallic acids dissolved in water to sip; or the solution may be applied directly to the bleeding tonsil. Perchloride of iron, which is sometimes recommended, should never be applied, as it produces clotting without arresting the hæmorrhage, conceals the bleeding spot, and often enough makes matters worse by inducing retching from the mechanical irritation of the fauces produced by the blood-clots. If ordinary styptic measures fail, we must seek for the bleeding point, and, if possible, the vessel from which the hæmorrhage flows should be seized and twisted with torsion forceps; or the sources of hæmorrhage may be touched with the galvano-cautery. Direct persistent digital compression has sometimes to be resorted to, and if even this fail, ligation of the carotid arteries, especially of the external carotid, remains as our last resource.

There still exists in the minds of the public and even of many practitioners a prejudice against operations on the tonsils; it is necessary, therefore, to refer briefly to some of the objections raised. First, it is urged in the case of children that they will "grow out of it," and that if matters are left to nature, the tonsils will spontaneously atrophy at puberty or soon after that time. It is true that in a certain proportion of the cases about two-thirds of the tonsils, by the age of twenty, either atrophy or cease to be inconvenient enough to urge the patient to seek advice; but in the remaining one-third of the cases this spontaneous disappearance does not occur, and therefore, although we may certainly tell the parents of a child suffering from enlarged tonsils that there is a chance of their atrophy after puberty, we must warn them that this event is by no means certain. But suppose our best hopes fulfilled, we have still to consider the great risks of serious and lasting consequences of great hypertrophy of the tonsils during the earlier years of life. If a child has not begun to suffer from the consequences of obstruction to the respiratory, alimentary, and auditory passages till the age of ten (and nearly half the total number of cases display marked symptoms before that age), and if we admit that his tonsils may atrophy by the age of eighteen, can it be fairly urged that eight years of constant interference with some of the most important functions of life, and that during the most important period of development, will not leave behind them lasting injury? The number of adult patients suffering since childhood from "throat deafness," and gradually getting worse, the configuration of countless faces seen in the streets, the defective articulation and intonation so often met with in people in society—all these defects tell their own tale and give the best reply to the question. And even if such sequels do not follow, the patient is liable to frequently recurring acute attacks of throat disorder.

Further, it is sometimes stated that the tonsils, even when hypertrophied, are protective against infectious disease; now it has been conclusively proved that tonsillar hypertrophy adds very greatly to the danger of infection, a point which we have fully emphasised in our opening remarks on diseases of the tonsils.

Removal of the tonsils never impairs the voice; on the contrary, in cases in which the masses of hypertrophied tissue are large enough to interfere with the normal vibrations of the column of air, and to divert it into an anomalous direction, and at the same time to interfere with the movements of the palatine arches and soft palate, and perhaps to maintain a chronic catarrhal pharyngitis, the voice will certainly be greatly improved in strength, quality, and timbre; although the removal of the tonsils will not of itself increase the range of the voice.

That removal of the tonsils has any tendency to result in sterility is a superstition so absurd that it is only worth mentioning to show that no belief is too foolish and groundless to be advanced against tonsillotomy.

In cases which urgently call for operative interference, not only are all the risks of local complications due to the enlarged tonsils removed, but there is almost invariably a rapid and marked alteration for the better in general health and development where these have been impaired. The appetite and digestion are improved, there is better aeration of the lungs, the child becomes fat, rosy-faced, bright and cheerful, and is a marked contrast indeed to the half-nourished, listless, anæmic, more or less deaf creature with open mouth and noisy respiration. The operation should not be postponed on account of the weakly condition of the patient; for though it seems reasonable to suggest that it would be well to wait until a course of careful dieting and general treatment have made the child stronger and better able to undergo operative treatment, we should remember that the local conditions are in themselves chiefly responsible for the adverse state of health, and that until the tonsils are removed but little amelioration can be anticipated; whereas the tonic treatment which has usually been tried before and failed will be attended with very much happier result after the operation, or, indeed, is usually rendered unnecessary, thereby. We have never in the whole of our experience seen any benefit derived from a postponement of the operation in the class of cases now under discussion.—F. S. and W. W.

REFERENCES

1. ALLBUTT and TEALE. *On Scrofulous Neck.* Lond. 1885.—2. BOSWORTH, F. *Diseases of the Nose and Throat.* New York, 1897.—3. BUSCHKE. *Deutsch. Zeit. f. Chir.* 1894, Bd. xxxviii. Hft. 4, 5.—4. BUTLIN, H. *Malignant Diseases of the Larynx.* Lond. 1883.—5. *Idem.* *Sarcoma and Carcinoma.* Lond. 1882.—6. CHEYNE, WATSON. *The Objects and Limits of Operations for Cancer*, Lettsomian Lectures, 1896.—7. CHIARI. "Ueber Lymphosarkome des Rachens," *Wien. klin. Woch.* 1894.—8. CORNIL. *Acad. of Med.* May 14; *La Semaine Méd.* 1895, p. 234.—9. COURMONT. *Revue de méd.* Sept. 1894.—10. DIEULAFOY. "Masked Tuberculosis of the Tonsils," *Med. Week*, London, 1895, p. 234.—11. FRÄNKEL, B., and MACINTYRE, J. "The Infectious Nature of Lacunar Tonsillitis," *Brit. Med. Journ.* 1895, vol. ii. p. 1018.—12. HALL, F. DE HAVILLAND. *Diseases of the Nose and Throat.* London, 1894.—13. KRUECKMANN, EMIL. "Ueber die Beziehungen der Tuberculose der Halslymphdrüsen zu der Tonsillen," *Virch. Archiv f. pathol. Anat. etc.* Berlin, 1894, No. xviii. Bd. 138, Hft. 3. —14. LANGENBECK. *Archiv für klinische Chirurgie*, vol. xlii. 1891, p. 325 *et seq.* —15. LEWIN. "Klinik der Syphilis-Statistik," *Charité-Annalen*, Berlin, 1874-77. —16. MACKENZIE, MORELL. *Diseases of the Throat and Nose*, vol. i. Lond. 1884.—17. M'BRIDE, J. *Diseases of the Throat, Nose, and Ear*, 2nd ed. Edin.—18. "Malignant Disease of the Larynx, Discussion on the Indications for Early Treatment of," *Brit. Med. Journ.* 1895, vol. ii. p. 1029.—19. NEWCOMB, J. E. "Ludwig's Angina," *New York Med. Journ.* Nov. 23, 1895.—20. NEWMAN, DAVID. *Malignant Disease of the Throat and Nose.* Edin. 1892.—21. NICHOLLS, J. E. H. "Sequelæ of Syphilis in the Pharynx and their Treatment," *Trans. Amer. Laryng. Assoc.* 1896.—22. RETTERER, E. "Sur le développement des tonsilles chez les mammifères," *Compt. rendu Acad. des sciences*, Paris, 1885, ci.—23. *Idem.* "Origine et évolution des amygdales chez les mammifères," *Journ. de l'anat. et physiol. etc.* Paris, 1888, vol. xxiv. —24. SCHLENKER. *Virchow's Archiv*, vol. cxxxiv. pp. 161 *et seq.* and 247 *et seq.* 1893. —25. SEILER, CARL. *Diagnosis and Treatment of Diseases of the Throat and Nasal Cavities.* Philad. 1883.—26. SEMON, F. "The Indications for Uvulotomy," *St. Thomas's Hospital Reports*, 1882, p. 80.—27. *Idem.* "Indications for and Method of Removal of the Tonsils," *St. Thomas's Hospital Reports*, Lond. 1883, new series, xiii. —28. SOKOLOWSKI and DMOCHOWSKI, and SENDZIAK. *Journ. of Laryng.* 1895, p. 287. —29. STOEHR, PHILIP. *Biologisches Centralb.* vol. iv. No. 12; and *Sitzungsbericht der physicalisch-medicinischen Gesellschaft zu Würzburg*, 1883, No. 6.—30. *Idem.* "Ueber Mandeln und Balgdrüsen," *Arch. für pathol. Anatom. etc.* Berlin, 1884, xcvii.—31. STRASSMANN and DMOCHOWSKI. *Med. Week*, 1895, p. 213.—32. TURNER, W. ALDREN. "The Innervation of the Muscles of the Soft Palate," *Journ. of Anat. and Phys.* 1889, vol. xxiii. part iv. p. 523.—33. WILLIAMS, P. WATSON. *Diseases of the Upper Respiratory Tract, the Nose, Pharynx, and Larynx.* Bristol, 1897.

III.—DISEASES OF THE LARYNX

LARYNGOSCOPY. Felix Semon and Watson Williams.
AUTOSCOPY AND SKIAGRAPHY OF THE LARYNX. Felix Semon.
ANÆMIA AND HYPERÆMIA:
ACUTE LARYNGITIS:
CHRONIC LARYNGITIS:
ŒDEMA:
HÆMORRHAGE:—F. de Havilland Hall.
TUBERCULOSIS. Felix Semon.
LUPUS:
LEPROSY:—Felix Semon and Watson Williams.
LARYNX IN ACROMEGALY. Watson Williams.
SYPHILIS:
PERICHONDRITIS:
DISEASES OF THE CRICO-ARYTÆNOID JOINT:
STENOSIS:
BENIGN GROWTHS (including PACHYDERMIA):
MALIGNANT GROWTHS:
NEUROSES:—Felix Semon and Watson Williams.

LARYNGOSCOPY

Inspection of the Larynx.—For this purpose a small mirror attached to a handle must be introduced into the back of the mouth, and a strong light thrown on the reflecting surface, which is directed obliquely downwards so as to reflect the image of the larynx. The small laryngoscopic mirror should be attached to the handle at an angle of about 120°. At least three sizes of these flat circular mirrors are desirable, of diameters of half an inch, one inch, and 1½ inch respectively, adapted, that is, to the size of the fauces at different ages.

The forehead reflecting mirror is concave and of about fourteen inch focus. It should be adjusted, by a freely adjustable ball and socket joint, to a forehead band or spectacle-frame carrier; the latter has the advantage of being more readily put on and off, and for hypermetropic or myopic observers spectacle glasses can be attached to the frame. In the centre it should have an oval opening, the long axis of which corresponds with the long axis of the observer's eye. It is essential that the central opening should come immediately in front of the pupil of the examiner's eye, and that the mirror be freely adjustable.

For a satisfactory examination a good light is of the utmost importance. Bright sunlight answers admirably when it is available; but it is usually more convenient to employ some form of artificial light which is wholly under control. In a darkened room a candle or oil lamp may suffice in some cases for diagnostic purposes; but an Argand burner, or, better still, the sixty-candle-power Welsbach incandescent burner, the electric, or the oxyhydrogen limelight is necessary for finer operations and for higher degrees of accuracy of diagnosis in many of the less gross or more obscure laryngeal affections, and for posterior rhinoscopy. The artificial light should be freely movable in every direction, so as to allow of ready adjustment and focussing of the light on the part to be examined.

The examiner should also accustom himself to the use of ordinary bright daylight concentrated by the forehead mirror upon the patient whose back is to a window, as this may give a better illumination than the poor light often afforded by the lamps available in private houses.

In proceeding to examine the larynx strict attention to the following method is advised. The patient is to sit on a common cane chair facing the examiner, who is similarly seated. The light should be placed on the left side of the patient, as close to the ear as is convenient, and so supported on a bracket, or a table, or held by an assistant, that the concentrated rays of light fall directly on the forehead mirror. The light returning from the centre of the forehead mirror and the laryngoscopic mirror when in place in the patient's mouth should be in the same horizontal plane during the examination; neglect of this fundamental rule is one of the commonest sources of failure in beginners. The patient with the head slightly thrown back should be directed to open his mouth, to breathe naturally, and to put out his tongue, which is to be immediately but gently grasped in a small towel by the examiner's left hand. The light having been concentrated at the back of the mouth, by adjusting the forehead mirror, the laryngoscopic mirror, lightly held in the right hand as one holds a pen, is introduced horizontally into the mouth till it reaches the uvula, when it is brought to an angle of about 90° by raising the handle and held steadily but gently against the uvula and soft palate but not so far back as to touch the posterior pharyngeal wall. The upper rim of the mirror should be about as high as the free margin of the velum palati. Before introduction the face of the laryngeal mirror should be warmed over the lamp so as to prevent the condensation of the moisture of the breath upon it. The proper temperature is obtained at the moment when the film of moisture, which at first forms on the reflecting surface, has disappeared; but to avoid the risk of introducing the mirror too hot, its temperature should always be tried on the back of the hand before it is introduced into the patient's mouth.

At first perhaps only the dorsum of the epiglottis may be seen in the small mirror; but by altering its angle the other parts of the larynx will be successively brought into view. While keeping the mouth widely open, the patient should be directed to sound "eh!" or "ēē," which causes the larynx to be raised and the epiglottis to be retracted so that the larynx is brought more perfectly into view. The vocal cords can then be seen approaching and diverging alternately in phonation and respiration.

It will be noticed that the laryngeal image is inverted antero-posteriorly, but that the right and left sides of the laryngeal image correspond to the same sides of the patient; there being of course no transposition of the reflected image in the horizontal plane.

The laryngoscopic image brings the following structures into view: the part first seen is the epiglottis; it appears in the upper portion of the mirror, more or less bent and saddle-shaped, so that it shows parts both of the upper and lower surfaces. The epiglottis varies greatly in form in different patients, being sometimes erect and only slightly curved, at other times pendulous, or very much bent and curled. The epiglottis is attached to the base of the tongue by three ligamentous folds: one central (superior glosso-epiglottic ligament), and two right and left (lateral glosso-epiglottic folds). The spaces between these folds are named the valleculæ. Below the epiglottis the pearly white vocal cords passing backwards to be attached to the arytænoid cartilages stand out clearly; between them is the triangular glottic chink through which a variable extent of the anterior wall of the trachea and sometimes even the bifurcation and the commencement of the bronchi may be seen. The true vocal cords are attached posteriorly to the processus vocales and to the anterior surfaces of the arytænoid cartilages; and anteriorly they are attached together in front in the angle of the thyroid cartilage forming the anterior commissure just below the projection or thickening called the cushion of the epiglottis. Along the outer sides of the vocal cords, and on a slightly higher level, lie the pink ventricular bands. In some cases, especially if we tilt the mirror laterally, the opening of the sacculus laryngis, or ventricle of Morgagni, can be seen on each side as a rim or chink between the ventricular band and the vocal cord. The arytænoid cartilages are seen as rounded swellings in the lower part of the image; between them is the inter-arytænoid space or fold forming the posterior wall of the larynx. The folds of mucous membrane stretching on each side between the epiglottis and the arytænoid cartilages are the arytæno-epiglottidean folds; and posteriorly, just in front of the arytænoid cartilages, the cartilages of Wrisberg and Santorini can often be recognised in the outline of these folds. Between the arytæno-epiglottidean folds and the prominence of the great cornu of the hyoid bone are the pyriform sinuses or hyoid fossæ.

In making a laryngoscopic examination we first observe (*a*) the colour of the various parts; secondly (*b*), the form and contour; and lastly (*c*), the functional activity of the vocal cords during phonation and respiration. As regards the colour, the epiglottis should be slightly yellowish and the rest of the laryngeal mucous membrane pale pink or red, while the vocal cords are, normally, pearly white or very slightly pink, though they are often of a more pronounced reddish colour, particularly in male professional vocalists. The vaso-motor changes in the larynx are very rapid: on first introducing the mirror, anæmia may be present; this on a second inspection may have given place to the normal tint, and on the third to hyperæmia. As isolated anæmia of the larynx is a valuable diagnostic sign, this inconstant condition should be carefully noted on the first inspection, while the structural alterations and the movements of the vocal cords may be left to a later observation. The structural alterations to be noted are tumefaction, ulceration, abscess, œdema, new growths, foreign bodies, malformations, and dislocations of the arytænoid cartilages. Any unevenness of the vocal cords should be particularly noted. Finally, the position and mobility of the cords will engage attention. No definite conclusion concerning the mobility of the vocal cords can be gained, as a rule, unless the larynx be examined both during phonation and deep inspiration. The neglect of this fundamental rule often results in overlooking laryngeal paralysis. During quiet respiration they should lie midway between adduction and abduction, "the position of rest or quiet respiration"; this is not the same as the "cadaveric" position in which the glottic chink is narrowed, for the wider aperture of rest, as has been shown by one of us (F. S.), is maintained by a persistent reflex tonus of the abductors. On phonating "eh! eh!" the vocal cords should come into symmetrical apposition in the middle line; the arytænoid cartilages at the same time being approximated by the arytænoideus muscle so as to obliterate the interarytænoid space. During deep inspiration the cords are widely abducted, so that the glottic opening and the interarytænoid space are considerably wider than during quiet respiration. It is not enough simply to observe that the vocal cord moves out on taking a breath; it is important to note also whether the degree of abduction on deep inspiration amounts to the normal.

There are then four named positions of the vocal cords, namely, those of (α) quiet respiration, (β) deep inspiration, (γ) phonation, and (δ) the cadaveric position of death or complete paralysis.

Finally, it may be necessary to test the tactile sensibility of the larynx by means of a long curved laryngeal probe. The normal larynx is very sensitive, and on contact violent cough is immediately set up, particularly when the interarytænoid fold is touched. In anæsthesia this sign is absent.

Difficulties in laryngoscopy may be encountered; sometimes this is due to the faulty method of the examiner, sometimes to structural peculiarities in the fauces or larynx of the patient. The following faults should be avoided: undue haste, flurrying the patient and rendering him nervous, attempts at examination without having the light properly concentrated; clumsy introduction of the mirror, or introduction of a mirror either not properly warmed or made too hot; dragging on the tongue or pressing it against the lower incisors; omission to tell the patient to breathe quietly and naturally; holding the mirror too long in the mouth, and neglect of the various little manœuvres for bringing the larynx into view by getting the patient to tilt his head backwards or forwards as may be required.

A common fault is to hold the laryngoscopic mirror at the wrong angle, or too far forward, so that only the dorsum of the tongue and the anterior surface of the epiglottis are reflected in it. By placing the mirror somewhat farther back and less horizontally, a complete image will probably be obtained.

Difficulties may arise on the side of the patient. Of these the most common are: (α) Excessive irritability of the fauces, leading to gagging and retching on the introduction of the mirror. To overcome this the patient may suck ice for fifteen or twenty minutes before the examination, or a 2 per cent cocaine solution may be sprayed on the fauces. (β) The dorsum of the tongue may rise so much that either the mirror cannot be introduced, or its reflecting surface is out of view. If forcible protrusion of the tongue by the patient or taking a deep breath does not overcome this difficulty, the patient should be asked to hold his own tongue, while the examiner depresses it with a tongue spatula held in the left hand. Sometimes the best view is to be had by simply depressing the tongue without protrusion; and if the patient be tongue-tied or protrusion impossible, this procedure should be adopted in the first instance. (γ) The tonsils may be so enlarged that the usual mirror cannot be used; in these cases it may be possible to introduce a smaller one. If the uvula be excessively long, it may get in the way; this obstacle will be overcome by using a large mirror. (δ) The most serious difficulty is a pendulous epiglottis so overhanging the larynx that the anterior portion of the larynx is concealed from view, and perhaps nothing but the posterior border is reflected. There are several ways of overcoming this difficulty. In slighter cases the act of phonating "ēē! ēē!" or coughing with the mirror in place may suffice to raise the epiglottis; then the vocal cords may come into view. If this manœuvre fail, direct the patient to throw his head well back, and place the mirror nearer the posterior wall of the pharynx, and somewhat more vertically than usual, the observer's eye being well above the level of the patient's mouth. In a few cases, however, it is only possible to see the vocal cords by raising the epiglottis with a retractor. (ε) The patient may hold his breath from nervousness; but a little patience will soon overcome this difficulty. It is important to remember that in nervous patients the vocal cords, instead of being widely abducted on deep inspiration, may be partially adducted, so that to the careless or inexperienced observer they may appear to be affected with paresis of the abductors.

The chief congenital defects that are met with are a deep central notch in the free border of the epiglottis, which may extend so far downwards as to produce a bifid or double epiglottis, and a membranous web between the vocal cords, which in some cases extends backwards as far as the vocal processes. In a case observed by one of us (F. S.) the web was associated with coloboma iridis.

Finally, we would emphasise the great importance of bearing in mind that it is as necessary in laryngeal affections as in all local maladies to have due regard to the general condition of the patient; to his facial aspect, his gait, and the state of his pulse, heart, lungs, and so forth: neglect of this fundamental rule may lead to the gravest errors in diagnosis. Thus, for instance, acute laryngitis may be due to gout, or recurrent attacks of laryngitis to early pulmonary tuberculosis; while a persistent and troublesome cough may be the earliest manifestation of tabes dorsalis; not to mention the grosser laryngeal lesions that may baffle the diagnosis unless the facts of the previous history and of a general examination of other regions are taken into consideration; for example, in syphilitic disease.—F. S. and W. W.

Autoscopy of the Air-Passages.—Quite recently a method of direct inspection of the upper air-passages has been introduced by Kirstein of Berlin, for which the inventor proposes the name of "autoscopy." He has found that on depressing the tongue by means of a suitable spatula it is possible in many cases to obtain a direct view of the posterior parts of the larynx and of the trachea. Recent as the method is, it has been repeatedly modified by its inventor since its introduction; at first it was somewhat complex, and a tolerably expensive apparatus was needed; it has now been so much simplified as to demand nothing more than a suitable spatula; indeed it is nothing more than a modification of pharyngoscopy as practised from times immemorial.

According to Kirstein's latest directions the practitioner should stand in front of the patient, who sits in an ordinary chair with his head slightly raised, so that an inspection from above downwards becomes possible. The spatula should be gently but firmly applied to the root of the tongue (not to its front or middle parts), whereby a furrow is formed, along which in many cases it is possible, with suitable illumination by means of a frontal mirror, to look directly down into the larynx; the epiglottis being usually raised by the pressure on the root of the tongue. It appears most important to avoid the production of retching; previous cocainisation of the parts may be of use, particularly when a subsequent operation is intended. Should a long upper lip or a moustache obstruct the view, the practitioner's other hand may be applied to get the obstacle out of the view.

Opinions concerning the usefulness and applicability of the method are as yet rather conflicting. Kirstein and Bruns recommend it particularly in cases of children; and the former states that the larynx and the trachea of deeply chloroformed children can always be inspected in their entirety by means of the autoscope; whilst by the help of this method Bruns has actually succeeded in removing papillomata from small children by endolaryngeal operation.

Skiagraphy of the Larynx.—It is as yet impossible to foretell the ultimate value of Röntgen's X rays in the diagnosis of laryngeal diseases. That the method promises to be very useful for the discovery of such foreign bodies impacted in the larynx as are impenetrable to these rays, has already been said in the chapter on foreign bodies in the upper air and food passages. It may be hoped, however, that the method will be so much extended as to make it serviceable for the diagnosis of other affections as well, as for instance of anchylosis of the crico-arytænoid articulations; and it would prove an inestimable boon for this branch of our science, if by its means an early differential diagnosis could be arrived at between benign and malignant growths of the larynx. We may anticipate that malignant growths, from their infiltrating character, may offer greater obstacles to the passage of the rays than the benign; it remains to be seen, however, whether it will be possible so to perfect the method that these finer differences may become recognisable.—F. S.

Anæmia of the Larynx.—The larynx partakes in the general pallor of the mucous membranes which is seen in anæmia. Isolated anæmia of the larynx is not infrequently the precursor of laryngeal tuberculosis; it is therefore an indication which should be carefully watched.

Hyperæmia of the Larynx.—All inflammatory states of the larynx are preceded by hyperæmia; hence hyperæmia of the larynx is in general an indication of the catarrhal process. One exception, however, deserves attention, namely, that in a certain number of men who constantly use the voice, as in singing, the vocal cords become slightly hyperæmic without in any way affecting the purity of the voice.

Acute Laryngitis.—Acute catarrhal inflammation of the larynx.

As men are more exposed to the *causes* of acute laryngitis they suffer more from it than women. Sudden changes of temperature, especially if a fall occur in an atmosphere highly charged with moisture, have long been recognised as likely to produce the disease. Exposure to draughts or wet acts in a similar manner. These causes are especially active in people who live in hot rooms, who over-clothe themselves, or drink too much.

The over-use of the voice, as in shouting, screaming, or even in prolonged speaking or singing, is sometimes sufficient to start an attack of laryngitis. When several of the above-mentioned causes are combined, as for example when a man, who has been shouting or singing in a public-house, and drinking and smoking at the same time, goes out from a heated room into the cold night air, an attack of acute catarrh of the larynx is a common result. The inhalation of certain irritant vapours, such as chlorine, sulphurous fumes, or ammonia, or of steam, as when children drink from the spout of a kettle, the application of caustics to the larynx, and surgical procedures for the removal of growths in the larynx, may give rise to laryngitis.

In most of the acute specific diseases, especially in measles, small-pox, and influenza, acute catarrh of the larynx is a common symptom. The rheumatic, gouty, tuberculous, strumous, and syphilitic habits dispose to catarrh of the larynx.

Before dismissing the causes of acute laryngitis, it is most important to bear in mind the part played by defective nasal respiration in rendering the larynx vulnerable to influences which would otherwise be innocuous. It has been pointed out that laryngitis is of common occurrence in cyclists who keep the mouth open in their need of air. In many cases, again, the acute attack of laryngitis is grafted on a condition of laryngeal catarrh more or less chronic.

The *morbid appearances* in acute laryngitis differ in no respect from those seen in acute catarrhal affections of other mucous membranes. The only point about which there has been any dispute is on the occurrence of ulcerations in simple acute laryngitis. That superficial and symmetrically disposed ulcerations may occur in the vocal processes, the inter-arytænoid fold, and anterior commissure is now pretty generally admitted. They seem to be due to contact of the inflamed mucous surfaces, especially in violent coughing. The ulcers which are observed in measles, influenza, and whooping-cough are only the ordinary catarrhal ulcers modified in their course and appearance by secondary infection.

The *symptoms* of acute laryngitis depend greatly upon the severity of the attack, and the age and sex of the patient. In an adult suffering from an attack of moderate severity, the chief complaint is a feeling of heat and soreness in the larynx; the voice is hoarse and there is usually an irritating cough, with at first little or no expectoration; but after a time pellets of mucus, in some cases streaked with blood, are coughed up: in inhabitants of towns the sputa are usually pigmented with soot or other impurities. Should the expectoration be abundant and frothy, in all probability the bronchial mucous membrane participates in the catarrh. There may be hardly any symptoms indicative of general disturbance of the system, except perhaps slight pyrexia and malaise. In women attacks of laryngitis are more liable to occur at the catamenial period, and in cases of uterine disorder. This is another of the many instances of the connection between the vocal and genital organs which we have indicated. Women are more likely than men to become aphonic during an attack of acute laryngitis.

In the most severe attacks there is usually some pain or tenderness over the larynx; this is particularly the case in patients of a rheumatic diathesis. There may be some discomfort in swallowing. Adults rarely suffer from dyspnœa unless the case be complicated with œdema of the larynx. The constitutional symptoms are well marked, and there may be high temperature and increased frequency of the pulse and respiration. In children, the comparative narrowness of the glottis and their great proclivity to nervous reflex excitability add elements of danger which are almost entirely absent in the case of adults. A child may go to bed, apparently suffering from coryza and slight hoarseness, to awake in the night with a loud, croupy cough, urgent dyspnœa, and cyanosis. During the day the child seems much better, but at night there may be a recurrence of the croupy attack. The pulsus paradoxus has been found in children suffering from the dyspnœa of acute laryngitis.

Laryngoscopically the appearances of acute laryngitis vary very much. In some cases the cords have a pale pinkish colour; in cases of greater severity the cords may be of so red a hue as hardly to be distinguishable from the rest of the larynx. Occasionally the congestion of the cords is irregularly distributed; or the brunt of the attack may fall on one cord, the other escaping almost entirely. Usually some sticky mucus may be seen on the cords, and on inspiring after phonation the cords may momentarily stick together. Accompanying the congestion of the cords there is usually some amount of infiltration of the submucosa and muscles, so that on phonation there is a want of tension in the cords. In rare cases small, round, or oval abrasions or ulcers, to which attention has already been directed, may be seen on the free margins of the cords. The term *acute epiglottiditis* has been applied to cases in which the inflammatory mischief is more or less limited to the epiglottis. As previously mentioned, the sputa may be streaked with blood; if the amount of blood poured out is considerable, some writers would designate the case as one of hæmorrhagic laryngitis. In these cases streaks of blood may be seen on the cords, and occasionally small varicosities have been recognised.

Since the introduction of the laryngoscope the *diagnosis* of acute laryngitis is a comparatively simple matter; the only difficulty occurs in children in whom it may sometimes be very difficult to distinguish acute laryngitis from laryngismus stridulus, on the one hand, and on the other from membranous laryngitis. In adults the prognosis as regards life is almost invariably favourable; death from acute laryngitis hardly comes within the pale of practical medicine. As regards complete restoration of voice a somewhat more cautious opinion must be expressed; for occasionally cases occur in which some amount of feebleness or impurity of voice persists, even after the most persevering treatment. The laryngitis of influenza, for example, is of a severe type; the hoarseness is difficult to treat, relapses are frequent, and paralytic phenomena may occur. In children, as already mentioned, there is a certain amount of risk due to spasm of the glottis.

Treatment.—In the most severe forms of acute laryngitis occurring in adults it is advisable to keep the patient in bed, in a room of the temperature of about 65°; and if the external atmosphere be very dry, a bronchitis kettle may be employed to moisten the air of the room. The patient should be enjoined not to talk, and his food should be soft and unstimulating. Equal parts of hot milk and Ems or Seltzer water make a pleasant and soothing drink. In most cases sucking small pieces of ice, and an ice-collar or cold compress round the neck, will afford the patient much comfort. In other cases the inhalation of the fumes of nascent chloride of ammonium, or of compound tincture of benzoin in water at a temperature of 140° F., will be found very soothing I have given great comfort by spraying the throat by means of an oil atomiser with a 5 per cent solution of menthol in paroleine. If the cough is frequent and irritating, pastilles of cocaine and rhatany or the morphia and ipecacuanha lozenges may be used. Tabloids of chloride of ammonium or the Soden mineral pastilles will be found useful in relieving the dry and irritable condition of the throat. Internally the bowels should be kept open by saline aperients, and a diaphoretic mixture is generally of use. Should there be any delay in the disappearance of the symptoms the larynx may be painted with a solution of chloride of zinc—twenty to thirty grains to the ounce. If want of tone be a marked feature, faradisation, massage of the larynx, and the administration of full doses of strychnia will accelerate the cure. The importance of seeing that the nasal respiration is free must be insisted on.

In children, the use of emetics—such as ipecacuanha or sulphate of copper, or apomorphia (gr. $\frac{1}{35}$ to $\frac{1}{30}$) injected subcutaneously—is useful in removing secretions. As a rule, hot compresses, or sponges wrung out in hot water and placed over the larynx, give more relief than the applications recommended for adults. The tendency to spasm should be controlled by the use of bromide of potassium or chloral. Where life is threatened by asphyxia, intubation or tracheotomy should be performed.

Chronic Laryngitis.—Chronic laryngeal catarrh. Inasmuch as all the causes of acute laryngitis are capable of exciting chronic catarrh, provided either that they are less active or the individual less prone to acute mischief, it will be only necessary here to lay stress on those which are peculiarly apt to set up chronic laryngitis. Indeed chronic laryngeal catarrh frequently follows an acute or sub-acute attack of laryngitis.

The first place should undoubtedly be given to over-use or faulty use of the voice; especially the use of the voice in the open air, in cold damp weather, or in an atmosphere vitiated by smoke, acrid fumes, dust, or other sources of irritation. Hence chronic laryngitis is most frequently met with in open-air preachers, costermongers, itinerant musicians, and stone-masons. Secondly, any interference with normal nasal respiration, either as a result of stenosis or of atrophic changes preventing the proper functional activity of the nose, is a potent cause of chronic laryngitis. A notable example of the connection between nasal and laryngeal affections is furnished by the occurrence of laryngitis sicca in cases of chronic atrophic rhinitis. Thirdly, syphilitic, tuberculous, malignant, or other diseases of the larynx, and the presence of neoplasms, are invariably accompanied by chronic catarrh.

The *morbid appearances* met with in chronic laryngitis are, for the most part, such as are commonly seen in a chronic inflammation of other mucous surfaces. It need only be said here that three more or less distinct forms of chronic laryngitis may be recognised. The first, or hypertrophic variety, as its name implies, is attended with hyperplasia of the mucous membrane of the larynx; this may be general or local. At times the ventricular bands are so much thickened as partially or entirely to obscure the vocal cords; or the cords themselves may be thickened and irregular, constituting one of the forms of Virchow's pachydermia. In the second, or atrophic variety, there is a shrinking or contraction of the mucous membrane; this is sometimes associated with similar changes in the nose and pharynx. The third variety has been named "glandular laryngitis"; in it the mucous membrane is somewhat thickened, but the most marked feature is the enlargement of the racemose glands.

Of the *symptoms* of chronic laryngitis, that which necessarily attracts most attention is an alteration in the voice. This may vary from slight hoarseness to complete loss of voice. As a rule it is most marked in the morning, the patient usually regaining a certain amount of power after he has used his voice for a time. In addition to the hoarseness, the patient finds that speech requires more effort than under ordinary circumstances, consequently he soon becomes tired and the voice feeble. Cough is not a constant symptom; when it does occur it is usually harsh and dry, or accompanied by the expectoration of a few pellets of mucus. Abundant expectoration, as a rule, betokens participation of the trachea and bronchi in the catarrhal process; there are, however, cases of profuse secretion from the larynx to which the term *laryngorrhœa* has been applied.

In *laryngitis sicca* the patient, after repeated efforts, may succeed in bringing up dry crusts of inspissated mucus; and he may suffer from intermittent attacks of dyspnœa due to the formation of large dry crusts in the hypoglottic region of the larynx. In some cases the sputa are blood-stained, or pure blood may be expectorated. The patient frequently feels hot and uncomfortable in the throat, but rarely has actual pain. General symptoms are almost, if not entirely absent.

The laryngoscopic appearances of chronic laryngitis vary considerably In the slighter cases there may be only a want of the clear white hue of the cords in health; they have a dull grayish or pinkish colour, and they do not exhibit the vivid redness seen in some cases of acute laryngitis. Usually both cords are affected; but the inflammatory change may be confined to one cord, or even to a part of a cord. Accompanying the congestion there is a want of muscular tone, so that on phonation the vocal cords do not come into complete apposition, but an oval gap is left between them. Mucus may be seen on the ventricular bands and in the arytænoid commissure; and occasionally the vocal cords are momentarily stuck together by the viscid mucus. In the more chronic cases the cords are thickened and irregular, and erosions are sometimes seen; but anything like distinct ulceration is so uncommon that some authors deny its existence as a part of simple chronic laryngitis. As already mentioned, the larynx may exhibit the changes to which Virchow has applied the name of *pachydermia laryngis.* He describes two varieties: in the warty form the change is limited to isolated spots, chiefly in the anterior extremities of the vocal cords; in the diffuse form the vocal processes are chiefly affected. The most characteristic appearance is an oval swelling on one vocal process, with a corresponding depression on the other. In chronic subglottic laryngitis there is a hyperplasia of the connective tissue beneath the vocal cords; and on a laryngoscopic examination the lumen of the larynx below the cords is narrowed by a tumefaction which is of a red or pale gray colour. In some instances there is reason to believe that subglottic hypertrophy is a manifestation of rhinoscleroma. In laryngitis sicca crust may be seen in the larynx, especially at the posterior commissure.

The *diagnosis* of chronic laryngitis is easy, save under two conditions; the one is laryngeal tuberculosis, the other malignant disease of the larynx. Many cases of tuberculosis of the larynx begin with all the appearances of an ordinary chronic catarrh of the larynx; and it is the subsequent course only which unfolds the real nature of the disease. Hence the importance of utilising any assistance that can be afforded by the examination of the sputa for tubercle bacilli and by the detection of phthisical processes in the lungs. In people over forty, and still more in those over fifty, limitation of the affection to one cord, especially if there be thickening associated with impaired mobility of the cord, should lead to a guarded prognosis in view of the possibility of the disease being of a malignant nature.

Treatment.—The first two things to be done, if the treatment of chronic laryngitis is to be conducted on rational principles, is to order complete rest of the voice, and the removal, if possible, of the cause or causes of the disease. It will hardly be necessary to insist on the importance of giving the voice rest; but, unfortunately, the patients who most frequently require treatment are those who earn their living by the use of their voice, and who are consequently most reluctant to give up the use of it. Nevertheless, it is hopeless to expect a cure if the patient continues the excessive use of the voice. As regards the removal of the causes of this complaint, the patient must be instructed in the proper method of voice-production; the nose should be carefully examined, and any departures from the normal conditions should be remedied so far as possible. The general health of the patient should be attended to, and anæmia, dyspepsia, constipation, and any other ailments present should receive appropriate treatment. As regards local treatment, inhalations of creasote or of the oil of Scotch pine may do a certain amount of good; but the chief remedy is the application of astringents to the cords by means of the laryngeal brush under the guidance of the mirror. In cases of moderate severity solutions of chloride of zinc (twenty and thirty grains to the ounce) may be employed; but in severe and obstinate cases nitrate of silver answers better. It should be used in solutions of gradually increasing strength, beginning with sixteen grains to the ounce, until ninety-six grains to the ounce or even stronger solutions are reached. The application should be made daily at first, until a certain amount of reactive inflammation is set up; and then at less frequent intervals, and the solutions gradually decreased in strength. In cases where there is much thickening of the cords, lactic acid in 30, 40, or 50 per cent solutions yields excellent results.

During convalescence various astringent sprays, such as chloride of zinc (two grains to the ounce), iron-alum (three grains to the ounce), or the perchloride of iron (three grains to the ounce), will be found of assistance.

Pastilles of benzoic acid or of the chloride of ammonium are also of service. If, after the congestion has been removed, the voice remain feeble, electricity, in the form either of the continuous or interrupted current, should be applied percutaneously; and massage over the larynx is sometimes of service. Internally, strychnia in full doses has a powerful effect in improving muscular tone, and is consequently useful in cases in which the approximation of the vocal cords on phonation is imperfect. Much good often results from sending the patient to a spa, such as Ems or Aix-les-Bains, for a course of two or three weeks, followed by a fortnight's stay in some bracing locality.

In the treatment of pachydermia laryngis rest of the voice is absolutely necessary; alcohol and tobacco should be prohibited. Small doses of iodide of potassium or of the green iodide of mercury seem to have a beneficial effect in some cases. The inhalation of a 3 per cent solution of acetic acid, and painting the growth with the same fluid, are said to have yielded favourable results.

Œdema of the Larynx (not including acute septic œdematous inflammation).—Though œdema of the larynx does not represent a distinct disease, but a complication of various diseased states general and local, still on account of its danger to life, and for the sake of obtaining a comprehensive view of its clinical features, a separate section may well be devoted to its consideration. The name œdema of the glottis was originally applied to the condition in question. Inasmuch, however, as the glottis is a space and cannot therefore become œdematous, the term is inappropriate, the more so as the vocal cords, which form the boundaries of the glottis, are of all parts of the larynx the least often œdematous.

Etiology.—Two varieties of œdema of the larynx may be described, namely, primary and secondary, or passive, œdema. Primary œdema may again be subdivided into the simple or non-infectious variety and the infectious or septic variety. Simple or non-infectious œdema of the larynx arises as the result of traumatism—as from swallowing some hard or pointed body, the application of caustics to the larynx, the entrance of brandy (given perhaps during an attack of syncope) into the larynx, and swallowing boiling water.

A form of primary œdema of the larynx, associated with a similar change in the pharynx and on the skin, has received the name of *angio-neurotic œdema;* in cases of this sort there is an absence of any inflammatory cause, and the urine does not contain albumin. It usually occurs in early adult life, and most frequently in women. Œdema of the larynx is also seen occasionally as a result of the administration of iodide of potassium; and it is probable, from analogy with angio-neurotic œdema, that the salt causes œdema by way of some influence on the nerves. The curious feature about the iodic œdema is that it may come on after the administration of a few small doses. Other symptoms of iodism, such as headache and coryza, are commonly absent. The possibility of the occurrence of œdema of the larynx while the patient is taking iodide of potassium should always be borne in mind, as a considerable number of cases have been met with; and in two instances recorded by Fournier death occurred before tracheotomy could be performed.

The infectious or septic forms of œdema of the larynx depend upon the entrance of infective germs into the tissues in or around the larynx. This form, which includes purely œdematous as well as the sero-purulent and phlegmonous exudations into the tissues which are due to the action of these microbes, and comprises primary erysipelas of the larynx, has already been dealt with in the section on "Acute septic inflammation of the throat."

Œdema of the larynx may also be met with in the early stage of infectious diseases without previous ulceration; it has been seen, for example, in a case of hydrophobia; and as a complication of ambulatory typhoid fever it has caused death by suffocation.

The causes of secondary œdema of the larynx may be arranged under two heads—local and general. The local causes include all the diseases of the larynx, such as tuberculosis, syphilis, carcinoma, and the laryngitis of influenza, small-pox, measles, and especially any disease which sets up perichondritis. I have seen it arise and prove fatal as a complication of quinsy. It has been noticed as a result of isolated suppuration of one of the deep cervical glands, even before the pus has broken through the capsule of the gland.

The general causes of œdema of the larynx are those which are capable of giving rise to general dropsy, such as valvular disease of the heart, chronic pulmonary or renal affections, the cachexy produced by malaria or lardaceous degeneration, and, lastly, passive congestion of the vessels of the larynx, such as arises from growths in the mediastinum, bronchocele, enlargement of the bronchial glands, or any growth in the neck compressing the branches of the superior vena cava.

Pathology.—In œdema of the larynx, the epiglottis, the ary-epiglottic folds, and the ventricular bands are the parts chiefly affected, on account of the lax nature of their submucosa; whereas the vocal cords, which are more firmly attached to the subjacent tissue, are very seldom œdematous. In some cases, however, the œdema is infraglottic; this variety has occurred as a result of the administration of iodide of potassium. The exudation varies from a purely serous to a sero-purulent or purulent quality, and the fluid is sometimes blood-stained. The serous variety is met with in all kinds of diseases which give rise to general dropsy, and in passive congestion of the part. In the septic and inflammatory varieties the œdema is due to a sero-purulent or purulent infiltration. Unilateral œdema usually points to an inflammatory cause; partial œdema has also been noticed in the course of Bright's disease. In most cases of acute œdema, in which the immediate causes are not apparent, primary erysipelas of the larynx is the true diagnosis. In all probability in many cases infective germs enter the system through slight injuries of the root of the tongue, and the inflammatory mischief passes thence to the epiglottis.

The connection between œdema of the larynx and Bright's disease has been denied by some authors. Peltesohn has collected 210 cases of œdema, and in 25 cases there was disease of the kidneys. That there is a connection between the two seems certain, but the nature of it is not equally clear. Probably the presence of Bright's disease determines the onset of œdema where there is a lesion too slight to cause it under ordinary circumstances. Œdema of the larynx in connection with Bright's disease may come on very gradually; in some cases, however, the œdema may form the first symptom or sign of the disease. Œdema of the larynx has also been met with in diabetic and myxœdematous patients, and it has been known to cause death in the new-born infant. The intimate connection existing between the genital organs and the vocal apparatus is shown by the fact that attacks of œdema of the larynx may correspond with the catamenial period. According to Binz, œdema of the larynx, due to iodide of potassium, can only come on if there be already some breach of surface in the laryngeal mucous membrane. The angio-neurotic œdema described by Strübing depends upon an increased irritability of the vasodilator nerves. Osler has reported two fatal cases.

Symptoms.—One of the first symptoms of which the patient complains is the feeling of a foreign body in the throat; there is difficulty or pain in swallowing, and, owing to this, the saliva, which the patient tries to expel, accumulates in the pyriform sinus. The voice is at first somewhat thick and muffled, and in severe cases the patients may become almost aphonic. Owing to defective closure of the glottis patients easily choke on taking fluids. In some cases inspiration only is difficult and accompanied with stridor; this is especially the case if the ary-epiglottic folds are affected alone. If, however, the ventricular bands and the laryngeal aspect of the epiglottis participate in the œdema, then expiration is interfered with also.

On laryngoscopic examination the mucous membrane covering the affected part looks tense and pale, though the margins may have an inflamed appearance. If the epiglottis is involved, it becomes swollen and erect; and the swollen ary-epiglottic folds resemble plums in shape. If the œdema is of the subglottic variety, two red fleshy swellings will be visible below the vocal cords. In the absence of a laryngoscope the swollen condition of the epiglottis and ary-epiglottic folds may be detected by digital examination. Clinically two forms of œdema of the larynx may be distinguished; the acute form runs a rapid course, a high degree of dyspnœa has been noticed within fifteen minutes after an infliction of an injury to the larynx, and death has been known to ensue within a few minutes; in the chronic form the symptoms arise more gradually, but even in these cases a sudden exacerbation is not uncommon.

In œdema of the larynx running a fatal course the patient presents all the symptoms met with in death from suffocation.

Prognosis.—Thanks to the more general use of the laryngoscope, which leads to the earlier recognition of the disease and to the more prompt performance of tracheotomy, the outlook in cases of œdema of the larynx is much better than it was formerly. General œdema of the larynx is of course more dangerous than an œdema confined to one side of the larynx. The subglottic œdema met with in connection with caries of the cricoid cartilage is a dangerous variety. In estimating the risk to life in any particular case it is necessary to bear in mind the possible supervention of spasm of the glottis. Again, the prognosis may directly depend upon the cause of the œdema; the septic variety, for instance, is especially dangerous on account of its secondary results. The œdema due to chronic dropsy will usually disappear quickly if the general cause be removed.

Treatment.—In all cases of œdema of the larynx absolute rest in bed, in a room kept at an even temperature, with the air somewhat moist, is essential. The patient should be forbidden to speak, and, in order to diminish the difficulty in swallowing, the food should be liquid or semisolid. I have seen much benefit from feeding the patient per rectum.

Pellets of ice to suck and an ice-bag or Leiter's coil around the neck are more suitable than hot applications. To prevent the tendency to spasm, bromide of potassium may be given in 10 to 20-grain doses every three or four hours. Three injections of pilocarpin (gr. $\frac{1}{8}$) at intervals of twenty minutes have given excellent results; in one case all threatening symptoms disappeared fifteen minutes after the last injection. If, in spite of these measures, the œdema increase and dyspnœa become more marked, the larynx should be sprayed or painted with a 20 per cent solution of cocaine, and the œdematous parts freely incised with Mackenzie's guarded laryngeal lancet. Should this procedure not give speedy relief, no time should be lost in resorting either to intubation or to tracheotomy; usually the latter will be necessary, as the swelling of the soft parts prevents the introduction of the tube.

Free administration of the bicarbonate of sodium in cases of œdema due to the iodide of potassium will be found of service, provided the œdema be not of dangerous dimensions. In angio-neurotic œdema Strubing recommends ice and morphia, and scarification if necessary. Small doses of atropine may be tried.

Laryngeal Hæmorrhage.—In some cases hæmorrhage takes place into the laryngeal mucous membrane; in others there is a free escape of blood, and the blood may be seen to issue from an ulcerated vessel, or the two conditions may be combined. In acute cases of laryngitis it is not unusual for the sputa to be streaked with blood; this was especially the case during the influenza epidemic: to cases in which the bleeding is profuse the name *hæmorrhagic laryngitis* has been applied. Hæmorrhage from the larynx occurs more frequently in women than in men, especially in pregnant women and after parturition; cases in which it has coincided with the catamenia have also been recorded. Exposure to cold, violent cough and retching and strain of the voice are the chief direct causes of laryngeal hæmorrhage, and the issue is most likely to occur in persons with degenerate vessels. Laryngeal hæmorrhage is met with in purpura, leukæmia, chlorosis, the malignant fevers, and other diseases in which there is an alteration in the composition of the blood. There seems to be no connection between the occurrence of laryngeal hæmorrhage and pulmonary consumption.

Symptoms.—As a rule, laryngeal hæmorrhage is so slight that it does not appreciably modify the symptoms of the laryngitis which it accompanies; occasionally, however, the blood is poured out in considerable quantity, and the blood-clots, by blocking the glottis, may give rise to dyspnœa; an attack of coughing will dislodge the clots and render the breathing free until the clots again form. If the hæmorrhage should come on suddenly, while the person is talking or singing, the voice immediately fails, and a spasmodic cough, followed by expectoration of blood, is set up.

In cases in which the hæmorrhage is due to altered blood states, the laryngeal symptoms are overshadowed by the symptoms of the general disease. On laryngoscopic examination blood may be recognised as an extravasation under the mucous membrane, or it may be seen on the surface, sometimes forming clots; occasionally a perforating ulcer may be distinguished as the source of the bleeding.

Treatment.—If the bleeding be at all profuse, the patient should be kept absolutely at rest and should not be allowed to talk; he should suck small pieces of ice, and have an ice poultice or Leiter's tubes applied over the larynx. The larynx should be sprayed with astringent solutions, such as 3 grains of iron-alum and 10 minims of glycerine in an ounce of water. If the hæmorrhage can be seen to come from an eroded spot, this may be touched with the galvano-cautery. Inhalation of turpentine is said to be useful in checking laryngeal hæmorrhage. If the cough be troublesome, small doses of morphine must be employed to check it.—F. de H. H.

Tuberculosis of the Larynx.—*Causes.*—Laryngeal tuberculosis forms one of the most frequent complications of the same disease in the lungs, and, according to Heinze's pathological investigations, is met with in about 30 per cent of all cases of pulmonary phthisis. The occurrence of primary laryngeal tuberculosis is now definitely established by the results of a few post-mortem examinations, but it is an event of the greatest rarity. It is much more frequently met with in men than in women, and its more severe forms also occur more frequently in the male sex. It is seen at all ages, but occurs rather in the years of early manhood. The determining cause of the disease is the bacillus tuberculosus, and the disease may be either acquired or hereditary; unfavourable conditions of life play the part of favouring factors. What determines the occurrence of the laryngeal complication is not yet certain. Professional vocalists are certainly less frequently attacked than others. Whether the disease begin on the surface and penetrate into the lower tissues, or whether the reverse be the order of events, is not yet definitely settled: the former order seems to be the more probable.

Pathology.—The deposit of tubercles in the larynx is usually manifested by infiltration and pseudo-œdematous thickening of the tissues. This is most marked, as a rule, in the epiglottis, the arytæno-epiglottidean folds, the mucous membrane covering the arytænoid cartilages, and the interarytænoid fold. In another series of cases, however, the disease begins on the vocal cords or on the ventricular bands; indeed, no part of the larynx is immune against the invasion of tubercle. The stage of actual infiltration is often preceded by marked isolated anæmia of the whole mucous membrane of the larynx, usually associated with an analogous condition of the pharyngeal mucous membrane; and the anæmia is most noticeable on the epiglottis. In very rare cases tubercles themselves have been seen as small yellowish or grayish nodules in the midst of the general infiltration; the stage of their corpuscular existence, however, must be extremely brief, and in the great majority of cases the first sign of their presence is manifested by the small superficial ulcerations which result from their break-down. These ulcers quickly coalesce, extend in width and depth, and after a time give a worm-eaten appearance to the parts attacked. The epithelium, the mucosa, and submucosa having been destroyed, they extend towards the perichondrium and lead to perichondritis, caries, necrosis, and often to exfoliation of parts of the cartilages. Sometimes actual tubercular tumours, consisting of an aggregation of miliary tubercles and cellular infiltration of the mucosa and submucosa, as well as of general débris, are met with in any part of the larynx, and this even in cases in which there is no evidence of concomitant lung disease.

Symptoms.—The subjective symptoms of laryngeal tuberculosis are, according to the seat of the disease, either hoarseness and, in later stages, more or less complete aphonia, or pain, difficulty in swallowing, cough with more or less expectoration, and sometimes dyspnœa. Often all these symptoms are met with simultaneously. The most troublesome of these are usually cough, pain and dysphagia. Whilst all the symptoms named depend, as a rule, upon these local conditions, the cough may also, of course, be due to the concomitant pulmonary disease; moreover, the vocal troubles are not necessarily due to the swollen and ulcerated state of the vocal cords, but may depend upon implication of the right recurrent laryngeal nerve in pleuritic thickening at the apex of the right lung, or upon pressure of enlarged bronchial glands upon one or both recurrent laryngeal nerves, and subsequent paralysis of the corresponding vocal cord: the shortness of breath often observed in these patients is more commonly due to the concomitant pulmonary affection than to the laryngeal trouble; though in later stages it may be of laryngeal origin, taking its rise either in general œdematous swelling of the larynx or in implication of the crico-arytænoid joints, with adducted position of the vocal cords as the result of perichondritis. In very rare cases bilateral paralysis of the abductors of the vocal cords, due to pressure of enlarged bronchial glands upon the recurrent laryngeal nerves, may produce the same effect.

Objectively, the pallor of the mucous membrane, preceding any definite signs of actual tuberculous mischief, and persisting generally throughout all subsequent stages, is of diagnostic value. When met with in any case in which there is not general anæmia the patient's lungs must be minutely examined. More rarely the initial symptom may be some laryngeal congestion, which at first is indistinguishable from ordinary laryngeal catarrh.

When tuberculous infiltration takes place, and particularly when this pre-eminently concerns the epiglottis and the mucous membrane over the arytænoid cartilages, as in many cases it does, the appearances often become so characteristic as to enable an experienced observer to diagnose the existence of tuberculosis with tolerable certainty, independently of the condition of the lungs, which, however, will never be neglected. In such cases the epiglottis is changed into a pale, rounded sausage or turban-like body, many times its normal size, lying across the pharynx; thus inspection of the interior of the larynx proper is often prevented, whilst the arytænoid cartilages are changed into two puffy, pale, rounded or pyriform bodies, which, together with the epiglottis, completely fill up the image seen in the laryngeal mirror. The œdema is distinguished from ordinary œdema by its greater density. Later, the surface of these swellings, originally smooth and shiny, becomes completely riddled with small superficial ulcers, which quickly coalesce and give to all the parts affected the worm-eaten appearance already described. In other cases tumefaction first begins in the interarytænoid fold; and when ulceration occurs, small stalactite-like projections may be seen in that part. Again, in a third class of cases the infiltration and ulceration may begin on one or both vocal cords or ventricular bands, and sometimes the only laryngeal manifestation of tuberculous disease of that part consists in complete erosion of one or both the cords by ulceration. In later stages the whole laryngeal mucous membrane often forms one mass of ulceration, which does not remain superficial, but gradually spreads towards the submucosa, the perichondrium and the cartilages themselves. The epiglottis may be destroyed in part or entirely; often indeed a short, irregular stump is the only evidence of its previous existence. The arytænoid cartilages may become carious and necrosed, and are sometimes expelled in their entirety, a crater-like ulcer in the middle of a puffy infiltration indicating their previous seat; or in other cases partial or total anchylosis of the crico-arytænoid joint takes place, and the cartilage, together with the corresponding vocal cord, becomes fixed and immovable. Apart from the last-named cause of complete or partial immobility of a vocal cord in the course of laryngeal tuberculosis, such impairment may be the result also of (*a*) functional weakness of the laryngeal muscles, particularly of the adductors, which is sometimes met with even in the earliest stage of laryngeal tuberculosis; and (*b*) of pressure upon one or both recurrent laryngeal nerves. In this respect the right recurrent is more exposed in laryngeal tuberculosis than the left, owing to its anatomical situation close to the inner aspect of the apex of the right lung; in this position it is not rarely implicated in the pleuritic thickening which accompanies destructive processes in the apex itself.

The diagnosis of tuberculosis of the larynx is not often difficult; the pallor of the parts, the characteristic infiltration of the epiglottis and arytænoid cartilages, the worm-eaten appearance in the later ulcerative stages, taken together with the pulmonary signs, the presence of bacilli in the sputum, and the general symptoms attending tuberculous disease, will in most cases find a ready interpretation. Greater difficulties may be met with when the initial stage is manifested by simple catarrh only. It must be remembered that simple catarrhal laryngitis for a long time may accompany a pulmonary tuberculosis. The apparent catarrh, however, may affect one vocal cord only, in which case the experienced observer will at once suspect some graver constitutional disease. The affections with which laryngeal tuberculosis is most likely to be confounded are syphilis, malignant disease, and lupus of the larynx. With regard to syphilis, apart from the manifestations in other parts which accompany tuberculous laryngitis on the one hand, and syphilitic laryngitis on the other, it may be observed that tuberculous ulceration is usually preceded by a more or less prolonged stage of pseudo-œdematous infiltration; that the aspect of the parts, as already mentioned, is distinguished by its great pallor, and the ulceration by its worm-eaten and superficial character. The syphilitic ulcer, on the other hand, the result of the breaking down of a gumma, is produced much more rapidly, and shows its inflammatory origin by the area of considerable inflammation which usually surrounds it: further, it is usually solitary and often very large; its rapidly destructive tendencies also are greater than those of laryngeal tuberculosis. It must not be forgotten, however, that syphilis and tuberculosis of the larynx may occur simultaneously in one and the same individual; and that under such circumstances the aspect of the parts may be anything but characteristic. In such cases the complex nature of the laryngeal disease will be cleared up by the administration of iodide of potassium.

With regard to the differential diagnosis from malignant disease the age of the patient may be of some help: tuberculous laryngitis is most frequently met with in persons from twenty to forty years of age; malignant disease usually occurs after that period of life: but there are many exceptions to this general rule. Further, laryngeal tuberculosis is usually bilateral; malignant disease, in its initial stages at any rate, is almost always unilateral. Again, cancer of the larynx often forms a much more distinct tumour than laryngeal tuberculosis, and in the former case an area of intense, even œdematous congestion and inflammation frequently exists around the new growth. Considerable secondary infiltration of the cervical glands also points to malignant disease. Sometimes, however, the differential diagnosis, especially in the later stages when secondary perichondritis may mask the original manifestations of either disease, is one of considerable difficulty; and undoubtedly laryngeal carcinoma may coexist with pulmonary tuberculosis, so that even the discovery of bacilli in the sputum, and the presence of the usual constitutional symptoms, do not give a definite clue to the nature of the laryngeal disease. In such cases, which fortunately are very rare, the extirpation and microscopic examination of a small piece of the laryngeal tumefaction may be of assistance, although this test again is anything but infallible.

Finally, with regard to the differential diagnosis from lupus, it may be said that laryngeal lupus is rare, and as a rule associated with analogous lesions in the nose, pharynx, and on the external integument. Further, laryngeal lupus usually is not painful, and gives rise to dysphagia in the later stages of ulceration only. Its course also is much slower than that of genuine tuberculosis; and even during the ulcerative stage the occurrence of fresh nodules will assist in making a differential diagnosis from genuine tuberculosis. Bacteriological tests, of course, are of no value for the differential diagnosis in these cases.

The prognosis in cases of laryngeal tuberculosis depends upon the nature and extent of the concomitant pulmonary not less than of the laryngeal lesions. In advanced cases of both, needless to say, it is bad; but the general character of the prognosis is not nearly so hopeless nowadays as it was fifteen years ago. If the pulmonary lesions be still limited to consolidation of the apices, and if the laryngeal ulcerations be not too extensive and are situated in the proper interior of the larynx, nowadays one is enabled by a judicious combination of constitutional and local treatment to arrest the disease in not a few cases; although, of course, even if we have succeeded in bringing about cicatrisation of a tuberculous ulcer, we must always be prepared for fresh manifestations.

Treatment.—The constitutional treatment I now regularly employ consists in the administration of large doses of pure creasote in small gelatine capsules, containing each one minim of the drug, as first suggested by Sommerbrodt. The patient begins by taking one capsule three times a day immediately after meals, and at intervals of three to four days he increases the dose gradually from one to five capsules each time; so that finally he takes fifteen minims of pure creasote three times a day. Some practitioners give even much larger doses, but I have not found this necessary, and I prefer the long-continued use of the drug in moderate quantities. Some of my patients have taken between ten and twenty thousand capsules in the course of two to four years, and are doing very well under it. In a few cases, of course, an idiosyncrasy against the use of creasote may be met with, and in such cases carbonate of guaiacol may be tried; but on the whole the toleration even of large doses of the drug is very remarkable, and in the cases in which it is said to have caused digestive troubles these could often be traced either to the use of an impure preparation or to the use of the capsules between meals instead of immediately after food.

Locally, when the ulceration is limited, I employ, after previous cocainsation, applications of lactic acid varying in strength from a 20 to an 80 per cent solution. The drug is firmly rubbed into the ulcerated parts by means of Krause's forceps round which a small pellet of cotton wool is firmly wound. To ensure success the practitioner ought to remember that these applications are not to be made in the gentle fashion of an ordinary astringent application, but in that of the cleansing of a tuberculous joint. If the ulceration be at all deep, the application of the lactic acid must be preceded by scraping the base of the ulcers by means of Heryng's curette, exactly as one would scrape the granulating surfaces of a tuberculous joint after it has been opened. This means, however, ought to be practised only by operators fully conversant with more delicate intralaryngeal operations, for by an indiscriminate use of the curette more harm than good may be done. In not a few cases the results of this treatment, when properly carried out, are most gratifying. Should the ulceration be too much advanced, and the general condition of the patient be at too low an ebb to admit of energetic treatment, local sedatives—such as powders containing acetate of morphia, boracic acid and deodorised iodoform, or cocaine lozenges, or a cocaine spray before the meals—ought to be employed. In such cases it will usually be found necessary to increase the dose of the local anæsthetic after some time;

but as the main object of the treatment under such circumstances is to promote euthanasia, one need not be afraid of the increase. In the more hopeful cases, after completion of the local treatment and when cicatrisation has been obtained, it may be desirable to advise a change of air; and either a sea-voyage or a stay at Bournemouth, or Torquay, or any of the health resorts of the Riviera, of Southern Italy, or of the north of Africa may be advantageous. In accord with the experience of most practitioners in the Engadine, I have found that the existence of laryngeal complications is a serious drawback to residence at those high altitudes, however desirable it may be from the point of view of the pulmonary disease.—F. S.

Lupus of the Pharynx and Larynx.—*Causes.*—The nose and throat are involved to a greater or less extent in a large percentage of cases of cutaneous lupus; in a small proportion, however, this disease originates and may long exist in the pharynx and larynx, without the external integument or the nose becoming affected.

As regards the etiology of the affection, it is directly due, no doubt, to a specific bacillus; and the great majority of writers are agreed in regarding lupus and tuberculosis as one and the same disease under different conditions. But while the identity of the specific microbe of lupus and tuberculosis is generally, though not universally, admitted, the cause of the remarkable difference in the clinical conditions seen in these diseases, especially as it manifests itself in the mucous membrane of the upper air-passages, has yet to be explained.

Women are much more prone to suffer from lupus than men; it generally reveals itself between the ages of two and ten years. It is more liable to occur in persons of an inherited tuberculous proclivity, though lupous patients are themselves but rarely the subjects of ordinary tuberculous disease; nor does the particular affection itself show any marked tendency to hereditary transmission. The disease is in no way connected with syphilis, although frequently in its physical aspects it is hardly distinguishable from the lesions of syphilis.

The nodules and tumefaction which are characteristic of lupus consist of a cellular new growth in the mucous membrane in which giant cells, and occasionally bacilli indistinguishable from tubercle bacilli, may be found. When the deposit first manifests itself on the uvula or on the free border of the soft palate, we may find localised tumefaction, generally of distinctly heightened colour, less marked and more limited than in syphilis or acute pharyngitis, but differing in aspect from the anæmia premonitory of tubercle; sometimes the deposit appears in mucous membrane apparently healthy. In course of time, smooth, hard nodules appear varying in size from a pin-head to a split pea, and generally of a rosy pink colour.

The nodular deposit greatly deforms the parts; and when arising in the uvula or soft palate the distortion and twisted appearance of the affected structures may be well marked.

Soon the nodules become softer and characteristically "apple-jelly-like" in appearance, and then as a rule ulceration begins. The ulcers present a serpiginous worm-eaten appearance, with defined hard or soft, granular and prominent margins, and a velvety, red, dry, indolent base. The process of ulceration progresses very slowly, healing in one direction while spreading in another; and periods of increased activity alternate with long periods during which the disease appears to remain in abeyance.

When the tonsils are involved, they become covered with irregular red nodules and pits of ulceration, but the course of the disease is precisely similar to the faucial deposits.

In the larynx, lupus generally attacks first the free margin of the epiglottis, which becomes tumefied; and the swelling gradually spreads to the arytæno-epiglottic fold and ventricular bands. The epiglottis becomes pale, "worm-eaten," and rough in aspect, and large portions may be completely lost. The vocal cords are usually the last part to be affected, and so slow is the progress of the disease that they often escape. When attacked, they become red and tumefied.

Symptoms.—As pain is practically never caused by lupus, the pharynx and larynx are often invaded without any obvious symptoms until the destruction of the soft palate causes fluids to return through the nose on swallowing, or gives a nasal tone to the voice and renders articulation imperfect. From the invasion of the posterior commissure or the vocal cords the voice becomes hoarse and aphonic. Some degree of stiffness in the pharynx and slight soreness and tickling sensations may be felt in the pharyngo-laryngeal region. In the advanced laryngeal disease cicatricial stenosis and dyspnœa very often arise and may necessitate tracheotomy, but there is hardly ever any inflammatory exudation with acute dyspnœa; the laryngeal stenosis is always very slowly established, and ample warning is given of the increasing urgency of the dyspnœa. Perichondritis or necrosis of cartilages is excessively rare.

Diagnosis.—The coexistence of cutaneous lupus will seldom leave room for doubt as to the correct interpretation of the pharyngeal and laryngeal phenomena; nevertheless it is sometimes a very difficult matter to make the diagnosis sure. The difficulties in the earlier stages are very much increased if the pharynx or larynx is affected primarily; the differential diagnosis has then to be made from simple chronic pharyngitis or laryngitis, syphilis, tuberculosis, and carcinoma.

Chronic pharyngitis is attended with increased secretion, and the hypertrophied lymphatic follicles are confined to the posterior and lateral walls, while there is no distortion of the parts, and the absence of lupous tubercles is to be noted. In the earlier stages of syphilitic laryngitis, especially in the catarrhal form with or without superficial ulceration, in the later stages with diffuse infiltration, and more especially in hereditary cases, the laryngoscopic appearance and the age of the patient often fail to settle the diagnosis till antisyphilitic remedies have been tried. Yet even at first the aspect of the tumefaction, the distortion of the parts, and the slow erosion of the tissues without distinct and obvious ulceration, are generally enough to lead at any rate to a strong suspicion of the real nature of the affection. The fact that lupus usually occurs in the very young, is very slowly progressive, always with cicatrisation, and is almost never painful, together with the peculiar appearances of the growth, and the absence of wasting, fever, or quickened pulse, should rarely leave any doubt as to the differential diagnosis from genuine tuberculosis, which is characterised by general pallor of the mucous membrane, and numerous mouse-nibbled, pale ulcers covered with grayish, disintegrating tuberculous tissue, and is usually accompanied by considerable pain, especially in swallowing.

The prognosis as regards life is favourable, the chief danger being stenosis of the larynx; but this comes on so gradually, and is so little prone to be suddenly increased by perichondritis or œdema, that tracheotomy can almost always be performed in good time. Occasionally long-standing lupus of the pharynx and larynx ends in pulmonary tuberculosis.

In cases in which the disease is confined to the pharynx and larynx, and is accessible, good results may be obtained by vigorous treatment, and occasionally complete cures.

Treatment.—Patients affected with lupus should be placed under the most favourable hygienic conditions possible, and during the winter months should take cod-liver oil; while general tonic remedies such as the syrup of iodide of iron or arsenic should be exhibited from time to time.

As regards local treatment, the nodules and tumefactions should be scarified or curetted, and strong lactic acid (80 per cent) rubbed in after the same manner as we adopt in tuberculous disease of the larynx. This should be done once a week, successive portions being treated until the whole of the diseased area has become cicatrised and no nodules or ulcers are visible. The cases should be watched for at least a year after apparent cure has been effected; and any fresh manifestations of the disease should be similarly dealt with at once.

Isolated deposits may be destroyed by the galvano-cautery. In a case shown before the Clinical Society of London by one of us (F. S.) some years ago, lasting and complete cure of a very extensive laryngeal lupus had been obtained by persistent use of this form of cautery.

Stenosis of the larynx may be arrested for a time by intubation or by the passage of Schrötter's bougies; occasionally tracheotomy may be unavoidable.

Leprosy of the Larynx and Pharynx.—For a general account of this disease and its causation the reader is referred to the article "Leprosy" in the second volume of this work.

Laryngeal symptoms.—The larynx is especially susceptible to leprosy, but the disease never appears upon the larynx primarily. It usually attacks this organ after it has invaded the skin, mouth, and fauces.

Leprosy of the throat may assume the tubercular or, very rarely, the anæsthetic variety. In either case the onset is extremely insidious, owing to the painless nature of the affection; and patients will sometimes declare that they have nothing the matter with the throat when examination reveals undoubted evidence that it has been established there for a long time.

Tubercular leprosy of the mucous membrane passes through three stages. In the first stage the uvula and soft palate, in which the alterations are usually first observed, become red and velvety in appearance, and the neighbouring tissues become affected by continuity or by separate foci of disease, so that the epiglottis and arytæno-epiglottic folds likewise become red, velvety, thickened, and hard, and appear as though coated with varnish. At this stage epistaxis frequently occurs, and the patient may complain of shortness of breath and a sense of tickling and dryness in the pharynx and larynx. In course of time the red, hard infiltration becomes soft, and the tissues somewhat œdematous, the redness soon giving place to pallor, till the affected regions are uniformly pale and resemble the anæmia of tuberculous disease; and when the infiltration and cellular elements become absorbed, the tissues appear, as Mackenzie puts it, as though infiltrated with tallow.

The second stage begins with the formation of the characteristic tubercles, and with the diminution or disappearance of the swelling and tumidity of the mucosa. At first they appear as small nodules of a whitish yellow colour, or white and almost glistening, varying in size from a pin's head to a split pea, isolated or in chains and groups, and sometimes surrounded by a hyperæmic areola. In this condition they may remain stationary for years, till the third stage is reached, provided the patient do not succumb to the general affection in the meanwhile. In this stage ulceration and disintegration of the tubercles take place. The ulcers at first are small and rounded, are elevated above the surrounding mucous membrane, and are compared by De la Sota to syphilitic mucous patches. Eventually they become deeper. The glottis assumes a rounded form, and the voice is lost. The fœtor of the breath at this stage becomes unbearable. The cartilages of the larynx become involved, the epiglottis presents a knobby aspect and may become hard and distorted, and in course of time the cartilages become necrosed and exfoliated.

The earliest indication of the throat affection consists in alteration of the quality of the voice, which at first becomes nasal, and with the implication of the larynx may be thick; yet the larynx may be extensively diseased without attracting the notice of the patient. Hoarseness or aphonia appears later from implication also of the vocal cords. Dyspnœa sometimes supervenes; and stenosis of the larynx, produced either by the nodular infiltration or œdema, may even necessitate tracheotomy.

The anæsthetic variety rarely affects the throat, and, according to Hillis of Demerara, it never does so until the cutaneous affection has existed for five years. The mucous membrane is smooth, the affected regions become anæsthetic, the velum palati is thin, tense, and paretic, and the arches of the palate assume a violet colour.

Diagnosis.—Leprosy has to be distinguished from syphilis, tuberculosis, lupus, and cancer; though laryngeal leprosy practically never occurs without cutaneous manifestations of the malady, and pharyngeal leprosy very rarely. Moreover, a leprous patient may be affected also with cancer, lupus, syphilis, or tuberculosis; or, on the other hand, patients suffering from any one of these diseases may be attacked by leprosy.

Syphilitic throat lesions have much in common with leprosy: first, in that they are usually painless, although the actual anæsthesia of the leprous larynx is not observed in syphilis; secondly, in the hyperæmia of the affected tissues; and, thirdly, in the tendency in the later manifestations of both affections for the cartilages to be attacked.

De la Sota states that the resemblance between syphilitic mucous patches and leprous ulcers is sometimes very close; but the dark reddish or coppery tint produced by syphilis contrasts with the grayish red that is observed in leprosy. Secondly, the anæsthesia in leprous patches is distinguished from the hyperæsthesia that may attend syphilitic lesions of the perichondrium. Thirdly, syphilitic ulceration does not go beyond a superficial erosion, while leprous ulcers, though true ulcers, yet are not so round and deep as tertiary syphilitic ulcers. They are much longer in formation, and do not respond to antisyphilitic treatment; indeed they are often made worse by it. The leprous nodules of the second stage are characteristic.

Tuberculosis in its earlier stages is attended with anæmia and hyperæsthesia of the parts; leprosy gives rise rather to hyperæmic infiltration. Leprosy is sometimes attended with febrile symptoms, but its onset is usually most insidious. The vocal cords are often affected early in tuberculous laryngitis; in leprosy the epiglottis and ventricular bands are generally invaded before the vocal cords. Leprous ulcers are more defined, less irregular than the painful tuberculous ulcers. Lupus may attack the larynx primarily, and De la Sota points out that the absence of cutaneous lesions is therefore a sufficient distinction from leprosy. Lupus arises in a healthy mucous membrane; the leprous tubercles are always preceded by a reddish coloration, which afterwards turns white. Leprous tubercles are white, soft, and variable in size. They appear in the form of a chain or a rosary, and their sensibility may be normal, diminished, or entirely abolished; lupous nodules are of a rosy or reddish hue, hard, resistant, and elastic, larger in size than those of leprosy, and, though indolent, of normal sensibility. Leprous ulcers are superficial, have indistinct edges, and suppurate but little; those of lupus have hard, elevated borders, a narrow sinuous fundus, and an abundant secretion. The scars in the two affections are not dissimilar; but those of leprosy are insensitive, while those of lupus retain the normal sensibility of the part affected.

The bright red colour of cancerous nodules of the larynx, which fades on pressure, contrasts with the dirty red, whitish, or yellowish opaque tubercle of leprosy. Cancerous tubercles may be associated with lancinating pain; and the irregular hard edges and irregular base of cancerous ulcers, with sanguinolent muco-purulent secretion, form a marked contrast with the superficial, dry, leprous ulcer.

Such, according to De la Sota, are the main points of distinction between the various diseases which may simulate leprosy of the throat.

Treatment, as a rule, can only be palliative, and is chiefly necessary in the stage of ulceration, when alterative and antiseptic solutions may be useful.

De la Sota has obtained improvement by the application of a 1 per cent solution of resorcin and of iodoform dissolved in ether, and by touching the diseased areas with a 10 per cent solution of chloride of zinc. George Mackern has had favourable results with the galvano-cautery in destroying the tubercles, especially those of the face and mouth; the eschars soon healed and the tubercles were not reproduced. When laryngeal stenosis gives rise to severe dyspnœa tracheotomy should be performed.—F. S. and W. W.

The Larynx in Acromegaly.—It appears, from a case observed by Dr. W. F. Chappell, that the pharynx and larynx may become involved in the hypertrophic manifestations of the disease. In a case of acromegaly in a man, Chappell found that external examination showed considerable enlargement of the larynx. Internally the epiglottis was thickened, the arytænoid cartilages and the ventricular bands were enlarged, but the glottic aperture was very small. As long as the patient remained quiet, respiration was unembarrassed, but during excitement the breathing was laboured, and the patient died in one of the attacks of dyspnœa.

The pillars of the fauces, soft palate, and uvula were much thickened, and the tonsils and lingual glands were hypertrophied.—W. W.

Syphilis of the Larynx.—*Pathology.*—Syphilitic disease of the larynx may be either inherited or acquired.

Inherited syphilis generally makes its appearance there either very shortly after birth or within the first years of life, when it usually takes the form of laryngeal catarrh or the milder forms of secondary syphilis; although occasionally even at that early time of life very severe manifestations are met with. It also shows itself about the age of puberty. In this later form tertiary phenomena are more frequently encountered.

Acquired syphilis of the larynx assumes the characters of the so-called secondary and tertiary forms, but "secondary" phenomena may arise and recur for many years after the primary sore, while "tertiary" forms may sometimes be met with even within a few months of the initial lesion. On the other hand, the tertiary manifestations may break out thirty or forty years after the primary sore.

The subdivision into "secondary" and "tertiary" forms is a very loose one, and, especially when the question of treatment arises, it must not be forgotten that a good many cases occupy intermediate stages of the disease. Sometimes we see tertiary lesions in the pharynx, and then, years after, very similar lesions in the larynx, long after the pharyngeal lesions have healed. The observations of Professor Lewin of Berlin have shown that in 20,000 cases of syphilitic affections which came under that author's observation during seventeen years in the syphilis wards of the Berlin Charité Hospital, in only about 3 per cent was the larynx attacked, and that of this number again the great majority (namely, about 87 per cent) belonged to the earlier and slighter stages of the disease; while in a small minority only (namely, in 13 per cent) were graver lesions found.

Syphilis of the larynx manifests itself in the following forms: (i.) Simple catarrh (Lewin's erythema); (ii.) Papules (condylomas, mucous patches); (iii.) Diffuse infiltration; (iv.) Gumma; (v.) Ulceration; (vi.) Fibroid metamorphosis; (vii.) Cicatrices, membranous adhesions; (viii.) Neoplasms; (ix.) Perichondritis; (x.) Paralyses.

Of these the first two are most frequently met with in the earlier and so-called "secondary" stages. Ulcerations are common to all stages, while the remainder belong to the group of "tertiary" phenomena. Lastly, all these lesions may occur in the inherited forms of the disease, though in congenital laryngeal syphilis the graver manifestations are decidedly rare.

The primary lesion is practically never seen in the larynx (though one case is reported by Moure), owing to the deep and inaccessible situation of the parts.

Syphilitic catarrh may occur as soon as six or eight weeks after the initial sore, and it is often associated with general secondary lesions. But it may appear two or three years or more after the infection, and continually recur for years, with the more serious manifestations of the disease. In no way does it differ in aspect from simple non-syphilitic catarrh, though it is remarkable for its persistency. We have not observed the distinction of colour which some observers have made, who allege that the colour is more dusky in syphilitic than in simple catarrh. The history and simultaneous appearance of syphilitic lesions in other parts—for instance, roseola and papular eruptions on the skin, or mucous patches on the tonsils and soft palate—generally lead to a correct diagnosis; though even when these are absent, the persistency of syphilitic catarrh and its resistance to the usual treatment for simple catarrhal laryngitis will arrest attention and lead to the suspicion of syphilis.

Mucous patches and condylomas are not often seen; in fact their occurrence in the larynx has been contested, and certainly the papulous syphilide is one of the rarest forms in which syphilis appears in the larynx. The circumscribed gray thickening of the infiltrated mucous membrane may occur on the epiglottis, especially on its lingual surface; or on the arytæno-epiglottic folds, posterior commissure, or the vocal cords. The patches are generally single or, if multiple, are not symmetrical. Superficial erosions—yellow, oval, circumscribed, and surrounded by an areola—may follow as the softened epithelium is abraded. As in the case of other secondary forms of syphilis, the specific catarrh and the other lesions just described tend to recur again and again for years The symptoms are hoarseness and sometimes slight expectoration.

Of the so-called tertiary forms, *diffuse infiltration* leads to tumefaction, which usually attacks the epiglottis, vocal cords, or interarytænoid fold, and sometimes causes considerable distortion of the affected parts, resulting in hoarseness and sometimes even in dyspnœa. The infiltration is due to a small-celled proliferation, which on the one hand may break down when small superficial ulcers are formed, or on the other hand may become organised into connective tissue so as to lead to a fibroid metamorphosis.

Gummas, before breaking down, are sometimes seen as smooth, red or yellowish defined swellings, generally single, and occupying the epiglottis—especially its margin or the laryngeal surface—the arytæno-epiglottic folds, the posterior wall of the larynx, or the ventricular bands; or they may be infraglottic. Histologically they are very similar to the diffuse infiltrations, but represent a more sharply circumscribed round-celled proliferation, developing as a rule in the submucous tissue, and thence extending towards the surface; so that the cartilages are only affected in the later stages, if at all. Very rarely does the infiltration begin in the perichondrium; if so, perichondritis may occur whilst the mucous membrane is still intact.

A gumma when about to break down generally becomes yellowish about the centre, ulceration follows, and the whole gumma then rapidly disintegrates from the centre towards the periphery, and a characteristic tertiary syphilitic ulcer results.

Ulcerations, if occurring in the secondary stages, are generally superficial, and most frequently are due to the breaking down of diffuse infiltrations.

Deeper ulceration belongs especially to the later manifestations of syphilis, and the ulcers present an undermined, slightly elevated, regular, sharply-cut margin, surrounded by a well-defined areola, and a floor covered by yellowish ropy muco-pus and necrotic tissue. The ulcer advances more in depth than in superficial extent with resulting cicatricial contraction, and often marked laryngeal stenosis and deformity of the parts affected. This is due to the well-known fact that the central portion of a syphilitic ulcer possesses the least healing capacity, and the peripheral portion the most; consequently the tough scars are often more or less stellate. When this scarring occurs at the level of the glottis, or in the trachea, the resulting contraction may produce considerable stenosis and dyspnœa. Sometimes a cicatricial membranous web is formed between the vocal cords or ventricular bands, which occludes the lumen of the larynx more or less.

Inflammatory hyperplasia and œdema often occur in the neighbourhood of acute and chronic ulcers of both periods, and around the gummas, leading to exacerbations of dyspnœa and other symptoms.

Fibroid metamorphosis of the diffuse infiltration occurs in some cases, the deposit becoming transformed into connective tissue. This form, in which sometimes frequent relapses occur, each of them followed by a renewal of the fibroid metamorphosis of the fresh infiltration, leads to the justly dreaded forms of general chronic stenosis of the larynx.

Papillary excrescences or neoplasms may be found in any part of the larynx, but most frequently project from the posterior commissure. They resemble those seen in tuberculous laryngeal disease, but consist of proliferated epithelium, and closely resemble the true neoplasms. Careful examination should prevent these mammillated outgrowths from being confounded with the steep and ragged margin of a syphilitic ulcer seen in profile.

Perichondritis is undoubtedly the most serious form of syphilitic disease of the larynx. It occurs in association with gumma, either by deep extension of the infiltration, or, more rarely, by the seat of the primary infiltration being between the perichondrium and the cartilage, whence it proceeds upwards and downwards. In both forms necrosis and destruction or exfoliation of the cartilage attacked is apt to follow. The epiglottis is often partly or wholly destroyed in this way, while the arytænoid cartilages may be expectorated, or the cricoid or thyroid cartilages laid bare till a necrosed portion comes away. But in rare cases the perichondrial infiltration, like the diffuse submucous infiltration, may escape the necrotic process, and undergo instead a form of adhesive or sclerosing metamorphosis characterised by thickening of the affected parts.

Paralysis of the vocal cords may be apparent only, and due to the fibroid thickening of the perichondrium of the arytænoid cartilages, to anchylosis of the crico-arytænoid articulations, or to fixation of the cords from contraction in their neighbourhood.

True paralysis may be of local or distant origin. The local causes are gumma in the crico-arytænoidei postici muscles, implication of nerve fibres in syphilitic deposits, or a syphilitic neuritis, which processes may not be associated with any obvious pathological condition of the larynx. Most frequently unilateral, these local causes of paralysis may be bilateral. But the paralysis of the vocal cords may be due to bulbar nuclear disease of syphilitic origin, or to implication of the nerve fibres in syphilitic pachymeningitis or gumma either at the base of the brain, or anywhere in their course to the larynx. In all these palsies the law of the proclivity of the abductors to succumb earlier than the adductors holds good.

The symptoms of laryngeal syphilis must obviously vary as the particular nature of the lesion, but the most remarkable feature common to them all is the almost entire absence of pain. Pain, however, is not invariably absent, and in rare instances it has been so severe as to lead to an erroneous diagnosis of malignant disease. It is not safe, therefore, to rely too much on the absence of pain. A gumma on the posterior surface of the cricoid cartilage, for instance, may be attended with considerable pain on swallowing. In the earlier manifestations patients complain of little but hoarseness, yet when the graver lesions of tertiary syphilis appear, there is sometimes a certain degree of soreness, while ulceration of the epiglottis may lead to dysphagia. The peculiar "raucous" hoarse voice, or even complete aphonia, is met with in secondary as well as in tertiary cases; and if the lumen of the larynx be encroached upon by deposits or by cicatricial contraction, dyspnœa will be the result. Cough is very rarely troublesome. The dyspnœa, as we have said, is liable to severe exacerbations from intercurrent hyperplastic syphilitic laryngitis and œdema.

Diagnosis.—It will be seen from the description of the various manifestations of laryngeal syphilis that it is impossible to lay down hard and fast rules for the diagnosis of the lesions; the objective and subjective symptoms alike depend (*a*) upon the seat, (*b*) upon the intensity of the syphilitic manifestation. As syphilitic catarrh has nothing characteristic in its appearance, the diagnosis of its specific nature will be derived from concomitant syphilitic lesions in other parts, and from its submission to antisyphilitic remedies, after it has resisted mere anticatarrhal treatment. Yet, of course, the larynx of a syphilitic person may be the subject of a simple laryngeal catarrh.

The diagnosis of tertiary lesions will depend on the laryngoscopic appearance, and on the history and concomitant lesions elsewhere, if any. It is, however, most important in regard to syphilis to trust to the evidence of the eye rather than to the history of the case. The patient very often does not know that he or she has been infected with syphilis; in many cases there is absolutely no history of anything to suggest this disease even when the patient is most desirous of affording all information on the point; in some cases, it is needless to say, the history of syphilitic infection is concealed.

The hoarse voice of children suffering from snuffles or broad condylomas about the anus will often lead to the suspicion that laryngeal symptoms are syphilitic. Most important is it to act on this suspicion in such patients when attacked with œdema supervening on hyperplastic syphilitic laryngitis, the symptoms being then very similar to those of membranous croup.

The two affections most likely to be confounded with laryngeal syphilis are (*a*) tuberculous disease, and (*b*) malignant disease. We have already spoken of the distinctive characteristics of syphilitic and tuberculous ulcers. In rare cases syphilis and tuberculous disease coexist in the larynx, in which cases there may be great difficulty in diagnosis. Again, when in syphilitic disease the lungs as well as the larynx are invaded, the real nature of the affection may be overlooked; but, first, the bacilli of tuberculosis will not be found in the expectoration; and, secondly, syphilis generally attacks the middle regions of the lungs, and, as a rule, not the apices.

In all doubtful cases iodide of potassium should be administered in considerable doses as a test of the nature of the affection.

As regards carcinoma, the appearances may be very similar in both affections, especially if the malignant new growth show itself in an infiltrating form. Here again the use of iodide of potassium, which test should be applied in all cases of a doubtful nature, will generally clear up all difficulty quickly; though it is true that a temporary subjective improvement under the use of iodide of potassium is often experienced even in malignant disease; the growth, however, steadily persists or increases in spite of the drug. The absence of glandular infiltration in the neck by no means excludes malignant disease, though, if present in considerable degree, it is more suggestive of malignant disease than of syphilis. In some cases, however, the diagnosis must remain for some time in abeyance, until careful watchfulness discovers further indications of its true nature.

Lupus may easily be confused with some syphilitic lesions; and in the absence of cutaneous lupus the difficulty in excluding syphilis, acquired or hereditary, is considerable: we may have even to wait in uncertainty for the result of antisyphilitic treatment.

The significance of scars, thickenings, distortions, and webs, left after the healing of syphilitic ulcers, will generally be interpreted correctly; but sometimes, in the absence of concomitant syphilitic phenomena or characteristic syphilitic paralysis of the ocular muscles and the like, there is the greatest difficulty in deciding whether the immobility of a vocal cord be due to anchylosis from previous syphilitic disease, or to true paralysis.

Treatment.—The general treatment of syphilis of the larynx is practically the same as for syphilitic disease in other regions, and is of fundamental importance. It is necessary, however, as we have already said, to dismiss the more rigid conceptions of the so-called secondary and tertiary forms of the disease; for some cases of what would certainly be called secondary affections will only yield to iodide of potassium, while in tertiary lesions, on the other hand, no improvement may follow the usual course of iodides, and alleviation is only to be procured by a mercurial course. Again, in other cases of tertiary syphilis, iodide of potassium produces a temporary amelioration only, and to prevent recurrence of symptoms the drug has to be continued for years. Finally, there are cases in which the alternating use of mercury and iodide of potassium produces the best results. Each case must, therefore, have its individual treatment; though no doubt the ordinary case of secondary disease is most benefited by mercury, and of tertiary disease by iodide of potassium in large doses.

In administering mercury our object should be to get the patient as quickly under its influence as possible, rather than to administer small doses over a long space of time, as advocated by some of the greatest authorities on syphilis.

The mercurial treatment recommended by Zeissl of Vienna is generally very satisfactory. Twenty grains of mercurial ointment are rubbed daily into various parts of the body: on the first day the ointment is to be applied to the skin of the neck over the larynx; on the second day, to the inner surfaces of both upper arms; on the third day, to the inner surfaces of both thighs; on the fourth day, to the inner surfaces of both forearms; on the fifth day, to the inner surfaces of both calves; on the sixth day, to the skin over both loins; and on the seventh day, to the skin of the back. This series of applications is to be repeated four or five times according to the exigencies of the individual case; each series being preceded and followed by a warm bath. In order to avoid mercurial stomatitis astringent and antiseptic gargles and vigilant cleansing of the teeth must be used during the whole time. Zeissl's method may be adopted in all stages of syphilis.

In tertiary syphilis we give iodide of potassium, beginning with at least ten grains three times daily, and increasing this to doses of thirty or forty grains. The depressing influence of iodide of potassium is rarely observed in syphilitic cases; and that in doubtful cases the patient thrives on the larger doses is a valuable diagnostic sign, apart from any improvement in the local mischief. In other cases a combination of mercury and iodide of potassium is most suitable. If the patient belong to the wealthier classes, Aix-la-Chapelle may be recommended, because with the simultaneous use of hot sulphur baths the mercury is pushed through the system much quicker than under ordinary circumstances, and general mercurialisation is avoided. The treatment of the congenital cases is the same as that for the acquired forms, but the doses are smaller in correspondence with the ages of the patients.

We very rarely use any local applications to the larynx in cases of syphilis. To this general rule an exception is made in cases of obstinate catarrh; and the foul ulcers of tertiary syphilis may require some mild antiseptic spray, while insufflations are sometimes useful in necrosing perichondritis. But in the great majority of cases constitutional treatment only is advisable; under it the local manifestations will heal quickly without local measures.

Stenosis of the larynx may be due to acute lesions, such as gumma with œdematous inflammation; and tracheotomy may be demanded. Yet as a rule energetic antisyphilitic treatment will soon obviate the necessity for relief in this way.

In chronic stenosis of the larynx, such as is due to chronic hyperplastic thickening, the formation of membranous webs, and so forth, tracheotomy or intubation may ultimately become unavoidable. As a rule, tracheotomy is to be preferred, as syphilitic stenosis is liable to recur after dilatation by Schrötter's bougies or by intubation tubes. O'Dwyer, however, has most successfully treated some very obstinate cases of extreme syphilitic stenosis by dilatation. Often only small tubes can be passed at first, but after leaving these in for twelve or twenty-four hours he finds it is generally possible to introduce larger ones, and eventually to obtain a permanent stretching of the cicatrisation.

Cicatricial web formations should be divided by cutting dilators, and intubation tubes worn till the edges have healed, so as to obviate reunion and reformation of the web. But the stenosis is very likely to return after a shorter or longer interval. In a few cases even partial laryngotomy and excision of the whole scar has been successfully performed under such circumstances, in order to enable patients to dispense with the canula.

Perichondritis of the Larynx.—*Causes.*—Perichondritis may be primary or secondary, but a primary origin is extremely rare. No doubt the vast majority of cases are secondary, although the immediate cause may be very obscure, and not infrequently, indeed, can be determined on post-mortem examination only. The term primary perichondritis should be restricted to those cases which are due to acute inflammation from cold, and are associated with more or less acute or chronic catarrhal inflammation of the larynx generally.

Of the causes of secondary perichondritis the chief are syphilitic, tuberculous, and malignant disease of the larynx; septic inflammation; typhoid and typhus fever; variola, diphtheria, and other acute infectious fevers; gout; injuries, including wounds and blows on the larynx; scalds; and those cases in which perichondritis is set up by the impaction of foreign bodies in the larynx, by swallowing hard masses of food, by the pressure of the larynx against the bodies of the cervical vertebræ in the continual dorsal decubitus of old people, or by the frequent passage of œsophageal bougies.

Pathology.—As a result of the scanty vascular supply of the perichondrium, and the absence of vessels in the cartilage itself, the separation of the perichondrium from the underlying cartilage by inflammatory exudation often results in suppuration followed by rupture of the abscess externally with exposure and necrosis of the whole or part of the cartilage—*suppurative perichondritis;* and undoubtedly this is the usual consequence of acute laryngeal perichondritis. Yet these very peculiarities in the vascular arrangement of the perichondrium and its cartilage would lead us to expect that the less acute forms of perichondritis should be followed by inflammatory degeneration rather than by inflammatory secretion, suppuration, and consequent necrosis. Thus we have a ready explanation of the relatively uncommon, but yet by no means rare *adhesive perichondritis* to which attention was drawn by one of us (F. S.) in 1880; in this form, without any free exudation between the inner layer of the perichondrium and the cartilage, the affected part becomes considerably thickened in consequence of an inflammatory new formation of dense connective tissue.

If an abscess form, it may rupture into the larynx, pharynx, trachea, or œsophagus; or it may discharge externally and form a laryngeal fistula. The exposed cartilage may maintain a chronic inflammation and discharge of pus for years; but sooner or later the necrosed cartilage is usually exfoliated, and may be coughed up or swallowed. When it has separated, the parts fall together and bring about great deformity of the larynx. Laryngeal affections in typhoid fever generally take the form of ulceration in the interarytænoid fold; probably some forms of perichondritis are secondary to these ulcerative processes, while in others it may be a primary process; but in both cases it usually attacks the posterior surface of the cricoid cartilage. Similar remarks apply to variola; in fact, apart from syphilis, tuberculosis, and malignant disease, the cricoid cartilage is the most frequently affected; and even in these diseases it is implicated often enough, either primarily or by extension of the inflammatory process from the arytænoid or thyroid cartilage. In tuberculosis the extension is most commonly from the arytænoid cartilages. If the arytænoidal perichondrium is involved, whether the inflammation take the suppurative form with consequent necrosis of the cartilage, or the more chronic adhesive form, the result is nearly always thickening of the capsule by tense connective tissue with or without degeneration or destruction of the crico-arytænoid joint, but with more or less complete mechanical fixation of the corresponding vocal cord. The strengthening of the capsular ligament of the crico-arytænoid joint externally by the tissue of the neighbouring perichondrium of the cricoid cartilage explains the very frequent occurrence of this mechanical impairment of the movements of the joint, even when the arytænoid cartilage itself does not seem to have participated in the obvious inflammation of the cricoid cartilage. In course of time a relatively slight degree of thickening of the capsule, which has nevertheless been attended by fixation of the arytænoid joint, may by contraction become less and less obvious; so that it is almost impossible from the laryngoscopic appearance to say whether a lasting paralysis of a vocal cord is nervous or mechanical in origin. One of us (W. W.) has observed such a condition following diphtheria in a case in which the mechanical fixation had been erroneously attributed to pressure on the left recurrent nerve by an aneurysm.

Symptoms.—Acute perichondritis may be ushered in with a sense of chilliness, or in some cases by a severe rigor, followed by a rise of temperature and other symptoms of febrile disturbance. In other cases the onset is less acute, and the earliest manifestation may be no more than a dull aching in the laryngeal region increased by pressure. If, as is usually the case, the posterior surface of the cricoid cartilage is involved, painful deglutition is often a marked symptom.

Dyspnœa results from excessive tumefaction on the interior surface of the thyroid or cricoid cartilages, even if it be only unilateral. If bilateral, both vocal cords are very apt to become fixed more or less in the phonatory position; in which case the voice may be preserved while the dyspnœa is urgent. The greater the opening of the glottis the less will be the dyspnœa, but the weaker the voice; it may fall in some cases to complete aphonia. Hoarseness is by no means necessarily present; but the diseases leading to perichondritis will as a rule affect the vocal cords also in greater or less degree, and thus hoarseness will be present in the majority of cases. In the secondary forms of perichondritis, which as we have said constitute the vast majority, the symptoms are generally more or less modified by the primary affection; especially is this the case in tuberculosis and malignant disease, and in the acute infectious fevers with mental dulness and general apathy. Syphilitic perichondritis, like all syphilitic affections of the larynx, is seldom painful. Objectively in the early stage the only alteration in the laryngoscopic appearance may be a smooth, or irregular, nodular, unilateral inflammatory swelling, with or without immobility of the corresponding vocal cord according to the part implicated. If the inner surface of the thyroid cartilage is the seat of the inflammation, the ventricular band is pushed up, forming a smooth tumefaction. If the cricoid cartilage is involved, there will be a subglottic swelling or tumefaction in the interarytænoid fold, or on its posterior surface, according to the part implicated.

When the arytænoid cartilage and its capsule are affected, they are generally red and swollen, but the tumefaction is not always obvious. Luxation of the crico-arytænoid joint is sometimes observed. Permanent anchylosis of the joint, or at least mechanical fixation, is the usual consequence (see p. 817).

If the exudation and swelling do not undergo resolution, suppuration with necrosis of the cartilage may occur, and crepitus may often be felt in manipulating the larynx; when the abscess has discharged, the bare necrosed cartilage may be detected with the aid of a laryngeal probe. In such cases purulent exudation, often associated with formation of fistulous tracts opening outside or into the œsophagus or other organ, may persist for years until the necrosed sequestrum is exfoliated; during this time the patient often presents a miserable aspect, and becomes greatly emaciated from the pain and dysphagia and want of sleep, while in syphilitic cases especially the accompanying fœtor is often very pronounced. Ultimately cicatricial contraction and marked deformity and stenosis of the larynx are the too common consequences of perichondritis, and the bilateral fixation of the vocal cords in the phonatory position may entail dangerous dyspnœa.

The diagnosis of perichondritis of the laryngeal cartilages presents many difficulties; for obviously in the earlier stages it will often be impossible to say definitely that the inflammatory exudation and swelling involve tissues deeper than the mucous membrane; and this difficulty does not always disappear when suppuration has occurred, unless crepitus can be felt or the bare cartilage detected. In tertiary syphilitic disease especially, we often have to wait the advent of definite signs of necrosis to determine the implication of the perichondrium; in tuberculosis, suppuration, apart from perichondritis, is rare.

The painful tumefaction with deep ulceration, and possibly profuse hæmorrhage, with general emaciation and constitutional weakness of advanced necrosis of the laryngeal cartilages, may be mistaken for malignant disease; on the other hand, the difficulty of eliminating perichondritis as a mere complication of malignant disease is sometimes equally great. The clinical history, the usual limitation of perichondritis to one cartilage, and, when the abscess has discharged, the less angry aspect of the swelling will assist us to arrive at a differential diagnosis: if serious doubts as to the real nature of the case are entertained, antisyphilitic remedies should always be administered nevertheless, and a portion of the swelling removed for histological examination.

The prognosis of laryngeal perichondritis is distinctly unfavourable, both as regards the restoration of the voice and the patency of the respiratory channel; moreover, the dangers to life are not inconsiderable. In the milder forms of adhesive perichondritis the movements of the vocal cords are rarely left unimpaired, while fixation of one or both cords results in marked alteration in the character and strength of the voice, and often in considerable dyspnœa. In the graver suppurative variety the patient may succumb to the disease before exfoliation of the sequestrum has occurred; and, even if he survive, the subsequent stenosis of the larynx very frequently necessitates tracheotomy and the permanent retention of the canula.

Treatment.—At the outset, during the stage of acute inflammation, cold should be applied externally to the region of the larynx, either by the ice-bag or by Leiter's tubes; and ice should be sucked. Leeches may sometimes be used with advantage on the affected side. The patient should be kept absolutely at rest, in the recumbent position if the thyroid or arytænoid cartilages are affected; if, however, the posterior surface of the cricoid cartilage be the seat of inflammation, the patient should lie on his side; under no circumstances should he be allowed to speak or whisper, so as to ensure absolute functional rest of the parts as far as possible. If the temperature be raised, three or four grains of quinine may be given at intervals; and for pain, if considerable, opium is useful. Food should be cold, soft and bland. The bowels should be freely moved. If the cricoid is affected and odynphagia is very pronounced, it is better to feed the patient by rectal enemas for a few days when it may still be hoped that active antiphlogistic measures may avert suppuration. In syphilitic cases iodide of potassium should be given internally, in considerable and increasing doses; and mercurial inunctions should be made in the laryngeal region externally.

There is always a danger of acute œdema coming on, with rapid increase in dyspnœa; when other measures have failed, asphyxia may sometimes be averted by intubation or by cocaine applications followed by scarification of the œdematous tissues; but if these means fail, tracheotomy must be performed.

When suppuration has occurred, with consequent necrosis, the dangers are considerably increased; therefore the patient's strength must be maintained by tonics and generous diet. As soon as possible the abscess should be evacuated.

After the acute stage has passed, the necrosed sequestrum should, if possible, be removed; for it tends to maintain conditions which are extremely adverse to the patient's health, and may become dislodged and either impacted in the glottic opening or pass into the trachea and bronchi with resulting septic pneumonia. Other radical operations, such as intubation and dilatation of laryngeal stricture, thyrotomy, removal of thickened parts, and so on, will also come under consideration. If the perichondritis be due to impaction of a foreign body in the larynx, it may become necessary, even during the acute stage, to perform thyrotomy and remove the offending substance. In a case observed by one of us (F. S.) this was done with complete success. In cases of fibroid stricture thyrotomy with extensive removal of the obstructing tissue has recently yielded very satisfactory results in several cases.

Diseases of the Crico-arytænoid Joint.—*Inflammation, Anchylosis, and Luxation.*—When we call to mind the physiological functions of the crico-arytænoid joint, namely, those of respiration and phonation, we may almost describe it, despite its small size, as one of the most important joints in the body.

Attention has already been directed to the very frequent implication of the capsule of the joint and its articular surfaces in perichondritis affecting the cricoid and arytænoid cartilages, which results either in suppuration and destruction of the joint, or in adhesive inflammatory degeneration with thickening of the capsule or true anchylosis of the joint.

Definition.—We call every degree of stiffness of the crico-arytænoid joint, which is produced by mechanical causes, an anchylosis of this joint; and we distinguish two forms, namely, first, the *true anchylosis*, in which the stiffness is produced by intra-capsular disease; and, secondly, the spurious or *false anchylosis*, in which extra-capsular changes lead mechanically to impairment of its functions. In some cases true anchylosis is a consequence of a long-existing false one.

Luxation of the crico-arytænoid articulation, first described by B. Fränkel, means a displacement of the arytænoid cartilage from the articular surface of the cricoid; in some cases both anchylosis and luxation coexist.

Causes.—Every true anchylosis is the product of an inflammatory degeneration of this joint, however slow and insidious the degenerative process may have been. The possible causes of anchylosis of the joint are as follows:—

(*a*) Anchylosis from local inflammatory causes; namely:—Perichondritis, suppurative or adhesive (by far the most frequent cause). Simple plastic laryngitis (?). Lesion of the joint by wounds, ulceration, luxations, contusions, and congenital causes.

(*b*) Anchylosis from constitutional causes leading to local affections; namely, typhoid fever, variola, syphilis, diphtheria, tuberculosis, gout, and excess of the physiological senile ossification.

(*c*) Anchylosis from purely mechanical causes leading to permanent immobility; namely, cicatricial contractions of the mucous membrane or of the muscles after injuries, enteric, syphilitic and other ulcerations (false anchylosis), neuropathic or myopathic paralysis, diaphragma or complete subglottic obliteration of the laryngeal passage, neoplasms.

The symptoms will depend, first, on the position taken by the arytænoid cartilages, and consequently by the vocal cords; and, secondly, on the amount of tumefaction and inflammation in and around the crico-arytænoid joint. Thus the joint may be fixed in any position, from that of deepest inspiration to that of phonation; and the arytænoid cartilage may be drawn even across the median line. These extreme positions are mostly found as the result of cicatricial contraction after syphilis and other ulcerative diseases; while in true anchylosis the implicated cord generally varies in position from the phonatory to what is called the "cadaveric" position, which lies midway between phonation and deep inspiration.

If bilateral anchylosis have occurred, the fixation of the cords is not necessarily symmetrical, but in the majority of cases it is unilateral.

Tumefaction is obvious in the majority of cases of true anchylosis; but in the spurious cases, even if true anchylosis should eventually supervene, it may be wholly absent. In short, immobility with tumefaction favours the diagnosis of mechanical impairment; immobility without tumefaction does not exclude this possibility. The swelling is sometimes very considerable, and may in itself be a serious impediment to respiration.

In complete anchylosis there will be complete immobility of the arytænoid cartilage and corresponding vocal cord; in incomplete anchylosis the mobility will be either restricted or jerky.

When anchylosis is combined with luxation of the joint, the position of the arytænoid cartilage will be abnormal, in addition to the swelling and immobility. In simple luxation the appearances are very similar to those presented by the last-mentioned combination, except that it is possible to reduce the luxation.

The chief subjective symptoms are alterations in the voice and dyspnœa. Each is determined by the position in which the affected vocal cord or cords are fixed. The quality of the voice may be unaltered or completely lost, though hoarseness, weakness, or diplophonia are usually observed. Dyspnœa occurs when both vocal cords are fixed near one another.

These symptoms are met with in infinite variety and degree; but they are so frequently modified by the primary disease that we can only draw attention to the main features.

Diagnosis.—When we consider the infinite variety of symptoms and objective appearances due to anchylosis, or associated with it, which may be encountered, and the many complications that so frequently coexist, it is easy to understand that in many cases a definite diagnosis of anchylosis cannot be made. More especially is this true of those cases which, not being associated with any obvious thickening of the arytænoid joint, exactly simulate palsy of the vocal cords of nervous or myopathic origin; on the other hand, the tumefaction of anchylosis may be mistaken for extensive effusion into and swelling of the soft parts covering the cartilaginous framework, with resulting temporary spurious anchylosis.

The most important points in favour of the diagnosis of anchylosis are the presence of tumefaction around an immobile arytænoid; abnormal position of the arytænoid cartilage; unilateral distortion of the contour of the larynx from cicatricial contraction or luxation; fixation of the vocal cord in the abducted position.

The prognosis, as to life, will depend on the nature of the primary disease; on the amount of tumefaction, and on the position assumed by the vocal cords: for instance, a position of bilateral abductor paralysis with the cords in the phonatory position is liable to end abruptly by acute asphyxia.

As to recovery of function, we must regard the length of time the anchylosis has existed, and again the nature of the primary disease. False anchylosis is more hopeful than true anchylosis; but if either have existed for a few months, very little hope can be entertained of complete recovery.

Treatment.—If the patient's life be in danger from asphyxia it may be necessary to perform tracheotomy before any measures for the treatment of the anchylosis can be undertaken; indeed, the nature of the primary disease may be such as to claim our entire attention, or may preclude the possibility of any successful therapeutic measures directed to the crico-arytænoid joint.

On the other hand, the subjective symptoms may be unimportant and unattended with any inconvenience; in this case it is better to leave well alone rather than run any risk of importing fresh and perhaps dangerous complications. Especially is this the case when true anchylosis has existed for a considerable time; then indeed treatment is useless.

Thus the indications for operative treatment are limited to the cases in which dyspnœa is a prominent symptom, in which there is no evidence of true anchylosis of the joint of long standing. We may then hope to obtain relief by mechanical dilatation by means of Schrotter's bougies, or by O'Dwyer's method of intubation continued for a long time.

But more help can be afforded by early methodical dilatation in preventing the occurrence of extreme stenosis and cicatricial contraction or luxation; and by timely treatment of more recent cases due to typhoid fever, syphilis, or to perichondritis from other causes.

Cheval states that he was able to reduce a recent simple luxation of the joint by means of a strong faradic current, a double electrode being applied to the posterior wall of the larynx so as to tetanise the inter-arytænoid and posterior crico-arytænoid muscles.

Stenosis of the Larynx.—*Causes.*—Laryngeal stenosis may be due to a variety of causes, namely:—

i. Infiltration of the tissues of the lining membrane, (*a*) by inflammatory exudation or œdema in the course of acute catarrhal or septic inflammations, scalds, typhus or typhoid fevers, measles and other exanthems, syphilis, tuberculosis, perichondritis, wounds, scalds and other injuries; or (*b*) by gummatous deposit, tubercle, cancer, lupus or leprosy.

ii. False membranes in croup and diphtheria.

iii. New growths, either benign or malignant.

iv. Congenital webs or adhesions between the vocal cords, cicatricial contraction following syphilis, lupus, perichondritis, typhoid fever, wounds, and so forth.

v. Bilateral abductor paralysis of the vocal cords, whether neuropathic or myopathic in origin, or due to mechanical fixation of the cords in the phonatory position.

vi. Foreign bodies.

The occurrence of stenosis of the larynx is incidentally referred to under the above-mentioned diseases, so that its characteristic symptoms and laryngoscopic signs need not be related again. We have now, strictly to confine ourselves to the intra-laryngeal operations for the relief of laryngeal stenosis, namely, intubation, dilatation by bougies, and so on, without reference to the question of the removal of the obstruction in the case of foreign bodies or new growths, or to the various antiphlogistic procedures and scarification that have been fully discussed elsewhere.

Treatment.—Stenosis of the larynx may be either acute or chronic.

In acute laryngeal stenosis requiring operative interference the choice lies between tracheotomy and intubation. If stenosis of the trachea be present at the same time, as in the case of diphtheritic membranes which have extended down the trachea and bronchi, or of compression of the trachea by an aneurysm or growth which has also caused bilateral abductor paralysis of the larynx, the question whether the dyspnœa will be relieved by any operative procedure confined to the larynx will arise. For the method of performing tracheotomy the reader will consult text-books of surgery.

Intubation of the larynx.—It is to Joseph O'Dwyer of New York that we owe the instruments whereby this method of treating laryngeal stenosis has been made practicable. His tubes for children are made of gilt metal, varying in length from 1½ inch up to 2½ inches for the age of twelve; the longer and larger tubes for adults are made of vulcanite. When the tube is in the larynx a flange at the upper end of it rests on the ventricular bands, and the rest of the tube lies below the vocal cords.

In proceeding to intubate young children the patient is closely wrapped in a blanket with the arms included, and is held sitting upright on the nurse's lap facing the operator. The mouth is kept open, and the head held steadily in the vertical position by an assistant. The operator, having passed the left forefinger into the larynx, hooks forward the epiglottis; the tube suited to the patient's age is then rapidly introduced on the obturator, which is attached to a handle held in the right hand, and is guided into the larynx by the finger which is hooking up the epiglottis, then the sliding rod on the handle is made to disengage the tube from the obturator, which is at once withdrawn, the left forefinger meanwhile fixing the tube and retaining it in position; finally this forefinger is removed. In the hands of a skilful operator the whole procedure occupies from three to five seconds. The tube should now be in position; but should it have been inadvertently passed into the œsophagus it may be extracted at once with the silk-thread loop attached previous to introduction. When the tube has been properly introduced the child gives a few strong coughs at first; but in the course of a few seconds the breathing is manifestly relieved, and the larynx very soon tolerates the tube. The loop should not be removed for ten minutes, as it tends to induce the coughing up of mucus and sometimes of small pieces of false membrane. Unless false membrane or other causes of obstructive dyspnœa exist in the trachea or bronchi, the embarrassed respiration gives place to quiet breathing, and the patient, who should always be placed in the steam bed, drops off into a calm sleep. Of course the patient is completely aphonic so long as the tube remains in the larynx; and though it removes glottic obstruction to breathing at once, inasmuch as the glottis cannot be closed, it acts exactly like a tracheotomy tube in rendering coughing less effectual.

The tube may be left undisturbed for five days or more if necessary, but sometimes it becomes more or less blocked by false membrane; in other cases it may be desirable, though rarely necessary, to remove the tube occasionally to allow the patient to clear the lower air-passages of tenacious mucus. For this purpose, and in order to enable the patient to imbibe a large amount of liquid food without discomfort, one of us (W. W.) makes a practice of removing the tube daily in older and docile children; for in them both intubation and extubation are rapidly accomplished without resistance, or the slightest risk ot injury to the larynx.

Extubation is more difficult than insertion of the tube. For this purpose the child is placed in the same position as for introduction, and expanding forceps, specially made for the purpose, are guided into the upper orifice of the tube by the left forefinger, previously passed into the larynx, till the instrument impinges on and fixes the posterior border of the flange; they are then opened so as to hold the tube firmly while it is rapidly withrawn. Neither intubation nor extubation should occupy more than fifteen seconds at the outside, as respiration is necessarily suspended during each process: if therefore an attempt be not promptly successful, it is better to try again rather than, by prolonged manipulation, to run any risk of asphyxia, or of setting up exhausting struggles for breath. It is needless to say that no force should ever be used.

If false membranes be present in the larynx the thread should not be cut short, but looped over the ear and fixed by plaister; or O'Dwyer's short tubes specially made for these cases should be used. These are short hollow cylinders of large calibre, which do not push the false membrane down. As they have no retention swell it is necessary to use the largest size possible. The symptoms of false membrane are sudden obstruction to the out-going air in expiration, and especially a flapping sound in coughing and a croupy cough when the tube is in.

The greatest care in feeding the patient is necessary to prevent the escape of food into the trachea. By intelligent children soft, semi-solid food can often be gulped slowly without risk. Liquid food may be taken if the patient can be induced to suck it through a tube, or to take it from an ordinary feeding-bottle while lying face downwards on the nurse's lap, or on a bed with its head pendent. If this does not answer, the patient must either be fed through a nasal tube, or nutrient enemas must be given.

Intubation should be performed early so as to prevent the engorgement of the lungs and the pulmonary collapse consequent on prolonged dyspnœa.

The advantages of intubation over tracheotomy in the treatment of acute laryngeal stenosis are—

(α) Its simplicity and painlessness, well exemplified by a case under one of us (W. W.), a child seven years old, who, having on former occasions experienced intubation and extubation at his hands, sat up and enabled him to extract the tube without being held or in any way restrained. On account of the relatively simple character of intubation, we can resort to this procedure much earlier than tracheotomy, and thus avoid all "cutting," to which parents sometimes will not consent.

(β) In children under five years of age the percentage of recoveries is considerably higher than after tracheotomy.

(γ) The intubation tube is more comfortably worn than the tracheotomy tube, in fact when in place it cannot be felt at all.

(δ) Respiration is conducted through the natural passages.

(ε) No anæsthetic is required as a rule, though cocaine may be used with great advantage. If the patient struggle much, especially in the case of an older child, chloroform should be given, and intubation or extubation performed in the recumbent position, rather than run any risk of exhausting the patient or of injuring the larynx.

The following difficulties may arise:—(i.) False membranes may occasionally be disengaged and crushed down into the trachea on introducing the tube. In such an event the tube can be withdrawn at once by the attached loop and the loosened membrane expectorated. (ii.) The tube may be coughed out and the dyspnœa return before help can be obtained. (iii.) Asphyxia may occur from blocking of the tube by false membrane. Such an accident can only occur in very feeble patients, as the tube, if blocked, is always expelled at once by a vigorous cough. Asphyxia may also arise from œdema above the tube, but it is a very unlikely occurrence. (iv.) Ulceration at the cricoid ring may be caused by an ill-fitting tube. (v.) Careless and rough introduction may make a false passage. (vi.) If the extubating forceps be opened widely outside the orifice of the tube as it lies in the larynx, instead of within it, the tissues may be torn as the instrument is withdrawn. (vii.) Difficulty may arise from subglottic stenosis at the narrowest part of the respiratory passages—the cricoid ring; but if the tube will not readily pass the obstruction here, a smaller one should be used. (viii.) If special precautions are not taken, "foreign body pneumonia" may arise from inspiration of liquid food. (ix.) Temporary aphonia sometimes persists for a few weeks after removal of the tube.

Intubation is chiefly practised for the relief of acute laryngeal stenosis in diphtheria and membranous croup; but it is sometimes to be recommended in recurrent laryngeal crises without abductor paresis; and in recent cases of crico-arytænoid fixation following typhoid fever, syphilis, and perichondritis from other causes, in which methodical dilatation by means of O'Dwyer's tubes or Schrötter's bougies may prevent the occurrence of cicatricial contraction.

One of us (W. W.) has observed several cases of acute laryngeal stenosis in adults (due to inflammatory swelling from various causes) in which a tracheotomy otherwise inevitable was obviated by intubation.

It is impossible from statistics alone to draw comparisons between tracheotomy and intubation; for whereas in diphtheria and acute inflammatory affections, at any rate, intubation is or should be adopted as soon as urgent dyspnœa is found not to be relieved by the use of the steam bed, calomel fumigations, and other means, tracheotomy is always delayed as long as reasonably possible. On the other hand, the early relief of intubation undoubtedly saves many lives that would otherwise be sacrificed, not by asphyxia but by pulmonary engorgement and lobular pneumonia Before the introduction of the diphtheria antitoxin statistics showed that under the age of five the results of intubation are better than those of tracheotomy; after this age the percentage of recoveries was *slightly* in favour of tracheotomy up to the twelfth year; while above the age of twelve tracheotomy yielded much better results.

But by the use of diphtheria antitoxin, not only has the mortality in cases of laryngeal diphtheria been very materially decreased, but with the relatively rapid relief of the laryngeal obstruction the difficulties and dangers of intubation have greatly diminished. The tube can in many cases be permanently removed in forty-eight hours, and, not infrequently, after a much shorter period. We should, therefore, give the preference to intubation over tracheotomy whenever it is practicable, secondary tracheotomy, speaking generally, being reserved for cases in which, for any reason, intubation has failed to give relief.

On the other hand, it should be borne in mind that the favourable influence of the diphtheria antitoxin injections on the results of intubation extends equally to tracheotomised patients, and that, inasmuch as the tracheotomy tube can often be safely discarded within a very few days, many of the secondary complications arising from tracheotomy are likewise avoided.

Chronic laryngeal stenosis.—In cases of chronic laryngeal stenosis, where the cause of the obstruction cannot be removed, tracheotomy is generally preferable to intubation, inasmuch as the latter entails loss of the voice, and the patient can only speak in a whisper; while after tracheotomy the patient very soon gets into the way of stopping the tracheotomy tube with his finger while speaking, and may continue to wear a tube for thirty years or more without discomfort.

O'Dwyer has obtained brilliant results in several cases of stenosis from chronic cicatricial contraction of the glottis following syphilitic disease. Often the tubes which can be passed at first are very small; but after leaving these in for twelve or twenty-four hours, it is generally possible to introduce a larger size, and so by patience and perseverance the largest tube can ultimately be passed; thus the cicatrix is more or less permanently stretched, and the dilatation can be maintained by passing a large tube once in three months.

The use of Schrötter's zinc bougies over a long period is sometimes successful in producing sufficient dilatation to obviate the further necessity for wearing a tracheotomy tube; in other cases, especially of membranous cicatrices between the vocal cords, intubation or mechanical dilatation, after section of the web by a cutting dilator, will yield favourable results: thyrotomy, with resection of the cicatricial tissue, is an alternative procedure suitable in a few cases.

Benign growths in the Larynx.—*Causes.*—Although benign growths of the larynx are of fairly common occurrence—a fact well demonstrated by the collective investigation instituted by one of us (F. S.), which resulted in bringing together no less than 10,747 cases observed by 107 laryngologists between 1862 and 1888—yet it is very difficult to assign their occurrence to any particular or definite causes. We are wont to look upon chronic laryngeal catarrh as the most prolific cause of innocent laryngeal tumours; but although chronic inflammatory affections of the larynx are common enough, we are not aware of any trustworthy observation of a new growth actually making its appearance in the course of a chronic laryngitis under the eyes of the observer, except, perhaps, the little inflammatory thickenings on the borders of the first and middle thirds of the vocal cords, known as "singers' nodules," often seen in singers and actors who have over-used their vocal organs. No doubt some laryngeal catarrh may be seen in association with benign growths; but this is a consequence of the presence of the neoplasm rather than the cause: moreover, in the majority of cases catarrhal processes are not present. Again, several cases of congenital new growths in the larynx are on record, and this fact, together with the relative infrequency of laryngitis in cases of benign growths, seems to exclude the probability that chronic catarrh is an essential factor in their occurrence. Whether occupation exercises much influence in the matter is also open to discussion. Excessive use of the voice has been held responsible for their appearance; but the very large number of benign growths occurring in young children, and their appearance not only in the newly-born but even in deaf mutes, show that such a cause cannot be widely operative; though we frequently meet with small circumscribed thickenings of the vocal cords, chiefly in singers who over-use their vocal organs or use them improperly. Men are more frequently attacked than women; yet the difference is not so striking as in the case of malignant growths of the larynx. No time of life is free from them; but they are most commonly met with between the ages of twenty and forty; and, next to this period, the first few years of life furnish the most cases. Though there have been instances of benign growths beginning in patients over seventy years of age, it is a good rule to look with suspicion on all growths which arise after the fiftieth year; as experience teaches that growths arising at this time of life are much more frequently malignant than benign.

As regards the various forms of benign growths in the larynx, in order of frequency they are as follows:—Papilloma, fibroma, cystoma, myxoma, adenoma, lymphoma, lipoma, angioma, ecchondroma, and growths consisting of normal thyroid tissue. Practically, of all these varieties only three are of common occurrence; namely, papilloma, fibroma, and cystoma: all the others are so very rare as to be but pathological curiosities.

Papilloma.—This is by far the commonest variety, constituting fully 39 per cent of all laryngeal growths. It is met with at all ages, but especially in young adults. Papilloma may be single or multiple, varying in size from a millet seed to a walnut, and of a white, delicate pink or red, granular, cauliflower-like appearance. These growths are usually pedunculated, not so often sessile, firm in texture, and do not readily bleed. Histologically they are composed of a number of vascular papillæ, covered by an epithelial layer. Their favourite seat is on the vocal cords; and of these, again, the anterior commissure and anterior thirds are more often attacked. Next in frequency come papillomata of the ventricular bands, where they are generally observed only in cases of multiple papillomatous degeneration. Sometimes they are seen projecting from the ventricle of Morgagni; in other cases they are attached to the arytæno-epiglottidean folds and to the epiglottis. In the latter positions they are very rare, and if observed in patients over fifty they should always be looked upon with suspicion of malignancy. Unlike epithelioma, their area is distinctly restricted; they do not infiltrate the surrounding tissue, and they are practically never seen in the interarytænoid fold. Early epithelioma of the larynx may very closely resemble a benign papilloma; the differential diagnosis is fully discussed on p. 837.

In syphilis and tuberculous disease of the larynx false excrescences are frequently observed in the interarytænoid fold or on the vocal processes; these and "pachydermia verrucosa" might be mistaken by the inexperienced for a benign growth if due attention were not given to their characteristic features, which are elsewhere described (p. 831).

Fibroma consists of the same tissue as the vocal cords, and originates in inflammatory thickening of their fibrous basis. It consists of connective tissue with an admixture of elastic fibres, is vascular, and may contain cavernous blood-spaces. These tumours are covered by epithelium, and serous infiltrations and hæmorrhages are common in them, especially in the softer varieties. The vascularity, particularly that of the sessile forms, is very considerable; and the hæmorrhage on removal is often much greater than in the case of papilloma.

Fibroma occurs in two forms, sessile and pedunculated, and in both forms is generally single, with a white, pink, cherry red or even bluish, smooth surface. It generally occupies the upper surface of the middle or anterior half of a vocal cord, and varies in size from a millet seed to a walnut. The multiplicity common in papilloma is not seen in fibroma. Sessile fibroma is almost always semi-globular; in the pedunculated form the stalk may be slender or stout, long or short. Sometimes the pedicle is long enough for the growth to hang down into the subglottic cavity, and to escape from sight except on forced expiration or cough, when it may be thrown above the level of the vocal cords; whilst on deep inspiration it is sucked into the subglottic cavity, and may completely disappear in it, the vocal cords on the next phonation meeting over it, so that the slight inequality in one cord, indicating the origin of the pedicle, alone betrays its existence. Fibromas vary greatly in size, from a pea to a hazel nut or more.

Cystoma.—As cysts result from obstruction in the duct of a muciparous gland, they generally occur where these are plentiful, and especially on the dorsal surface of the epiglottis. But they may occur in any part of the larynx where glands exist; and then they are found on the ventricular bands, or growing from the ventricle or the arytænoid region, and, in rare cases, even from the vocal cords. They are smooth, tense, globular, semi-translucent, covered with light red or grayish pink mucous membrane, and, if considerable in size, have blood-vessels coursing over their surface. Sometimes they attain so large a size as to be visible with the naked eye when situated on the epiglottis; and if arising in the larynx itself they may actually threaten suffocation.

The other forms of laryngeal benign growths, as already stated, are very rare; some of them, such as lymphoma and mycosis fungoides, need only be mentioned by name.

Angioma is generally unilateral and single, occurring in the sinus pyriformis, or on the ventricular bands, vocal cords, or epiglottis, of characteristic aspect, and composed of a mass of blood-vessels held together by a small quantity of loose connective tissue. The growth is red or purple in colour, and rarely exceeds a filbert in size. A case has been described by Semon and Shattock in which a malignant growth, originating from the left arytæno-epiglottidean fold, closely simulated an angioma (28).

Myxoma usually occurs on the vocal cords. It likewise is generally solitary, small, pink, or grayish white, sessile, translucent, and well defined. If pedunculated, the growth partakes rather of the fibro-myxomatous nature, and then may present a mammillated surface and resemble a papilloma in aspect.

Ecchondroma mostly arises from the cricoid cartilage. It has been observed growing from the epiglottis, thyroid and arytænoid cartilages. Ecchondromas are usually firmly attached, hard, sessile growths, presenting a smooth surface of irregular outline and covered with healthy mucous membrane.

Lipoma may attain considerable size. One removed by Sydney Jones from the right arytæno-epiglottidean fold partly projected into the patient's mouth, so enormous was the size it had attained.

Prolapse of the ventricle of Morgagni, though strictly speaking not a new growth, clinically resembles a laryngeal neoplasm so closely that it may be conveniently mentioned here. A smooth, pink, lobulated, supraglottic mass, generally unilateral, sometimes bilateral, is seen resting on the vocal cords, and corresponding to the opening of the sacculus, which, being inverted, of course no longer exists. That such an inversion should be possible seems hardly credible; yet several cases have been observed both during life and on the post-mortem table by trustworthy observers. It is most frequently seen in phthisis pulmonalis, and appears to result from atrophy of the thyro-arytænoidei muscles, and to be directly brought about by violent coughing. As it is useless to replace it, the projecting portion should be snared or excised. It should be borne in mind that the dislocation is exceedingly rare, and may be closely simulated by outgrowths from the ventricle.

The symptoms of benign laryngeal growths, it is needless to say, will vary according to their size and situation. By far the most frequent symptom met with, and indeed in most cases the only one, is alteration of voice. This explains itself when we remember that the vocal cords are the principal seat of these growths. The degree of vocal impairment will depend, of course, on the amount of interference with the free vibration of the vocal cords. Even a very small growth occupying the anterior commissure or the free border of the cords in their anterior third may greatly impair the voice or even produce complete aphonia; whereas growths which do not encroach on the free borders, or which are situated on the middle parts of the cords, may give rise to a much less marked vocal impairment; in some cases, indeed, no symptoms whatever occur.

When the growth is sufficiently large to encroach considerably on the glottic space, and to narrow the canal of the larynx, dyspnœa must result, and the degree of dyspnœa will of course depend on the degree of narrowing of the canal.

Cough is rarely a prominent symptom, but in very young children with papilloma it may be present and be croupy in character, as the growths are apt to excite some degree of laryngitis and glottic spasm. Pain is hardly ever felt, and only in a few cases, particularly of pedunculated growths, are strange sensations noticed, while spontaneous hæmorrhages practically never occur. Dysphagia may be present when a large growth is attached to the upper surface of the epiglottis.

The prognosis as regards life and health is nearly always most favourable, but the possible developments which these growths may take if left untreated must not be forgotten. We have already mentioned that papillomas occur either in the solitary or multiple form. In the former case, after having attained a certain size, they may remain stationary for a long time; but they are more likely to become gradually larger, and this is, indeed, the rule with the multiple forms; in this case they encroach on the glottic space and threaten asphyxia, an event which has indeed occurred in several cases.

Fibroma, after having attained a certain size, not rarely becomes stationary; in other cases, however, it continues to grow slowly, and may sometimes, after many years, cause serious respiratory difficulties. In a case of a large pedunculated fibroma recently observed by one of us (F. S.), suffocation occurred quite suddenly, probably from impaction of the growth in the glottis. No post-mortem examination was obtained.

Spontaneous expulsion of new growths has been reported very rarely indeed; so excessively rare is it that the prospect of it ought not to be held out to any patient. One of us (F. S.) has seen involution take place in the course of years in a few cases of growing children with small nodules, apparently fibromatous, on their vocal cords; but this, too, is certainly very rare. On the whole it may be said that benign laryngeal growths, when left to themselves, though they may become stationary at a certain period, are more likely to increase gradually in size; and papillomas do so sometimes rather rapidly. The prognosis from the therapeutic point of view is nowadays almost universally good, although the tendency of papilloma to recurrence must always be remembered. Also the prognosis as to the recovery of voice is, on the whole, very good, though in cases of sessile or very multiple growths some small vocal disturbances may remain behind after their removal. The one class of benign growths in which the prognosis ought to be very guarded, if not as to life, yet at any rate as to duration of disease and to subsequent function of the parts, are the cases of papilloma in early childhood in which it may be found necessary to perform prophylactic tracheotomy to prevent suffocation, or in which thyrotomy has been carried out for removal of the growth.

We must here refer to a question which has of late been the subject of a good deal of controversy, namely, whether benign growths of the larynx ever undergo malignant degeneration, and, if so, whether this tendency is increased by intra-laryngeal operative interference. This question could only be answered definitely by a critical review of a very large number of cases, and to this end the collective investigation (2) already referred to was instituted by one of us (F. S.) with the following result:—Of 10,747 cases of innocent laryngeal growths observed by 107 laryngologists, 8216 had been operated on intra-laryngeally; of these in 33 cases malignant degeneration was reported, that is to say, 1 degeneration in 249 cases; but on critically analysing the individual cases of reported degenerations, in 5 only was such degeneration found to have been quite or almost undeniable; and even if 7 further cases in which the degeneration was more or less probable be added to the number of the certain cases, the proportion of degeneration would be but 1 in 685 cases. The remaining cases of reported degeneration were of an exceedingly doubtful character, and in most of them it was probable that a diagnostic mistake had been made from the very beginning. Under all circumstances the occurrence of a malignant degeneration of a previously benign laryngeal growth must be considered as an event of the greatest rarity; and the very number adduced affords sufficient evidence that the alarm which has been raised concerning the influence of intra-laryngeal operation upon the occurrence of such degeneration is absolutely unfounded. A further proof of this conclusion is that a positively larger number of spontaneous degenerations in non-operated cases were reported in the collective investigation than of degenerations after removal; the percentage in the first class of cases was 1 to 211, in the second class

1 to 249. Of course we do not deny the possibility of benign laryngeal growths sometimes undergoing malignant degeneration like benign growths in other parts of the body; but there is no evidence that this is aided by intra-laryngeal operations. It is much more probable that cases are diagnosed as benign which were really malignant from the outset.

Diagnosis.—It is needless to say that the diagnosis of benign laryngeal growth can only be made by means of a laryngoscopic examination, as the symptoms consist almost entirely of vocal impairment and perhaps dyspnœa, the former of which may equally well be due to chronic laryngitis and numerous other causes, while both symptoms may be produced by syphilitic, tuberculous, or inflammatory disease, or by paralytic disorders. The differential diagnosis between benign growths on the one hand and these several diseases on the other is not usually difficult, though it is sometimes impossible to distinguish between benign growths and tuberculous tumours; sometimes indeed this can only be definitely settled by a microscopical examination of the fragment removed. The appearances presented by the various forms of new growth have already been sufficiently noted, and the very important question of the differential diagnosis between benign and malignant tumours is fully discussed further on (p. 837 *et seq.*).

Treatment.—A very few cases of benign laryngeal growths are best left alone; they are chiefly cases of small sessile fibroma situated on the vocal cords, and causing very slight symptoms. In such cases removal is sometimes exceedingly difficult, and in the endeavour to remove them there is a risk of injuring healthy parts in the neighbourhood and of bringing about still greater vocal impairment. These cases, however, are very exceptional, and in the vast majority it is not only desirable, but even necessary, on account of the symptoms, to remove the neoplasm. Astringent local remedies have been advocated, and it has been stated that growths have been made to disappear by their use; but we have never seen such a happy consummation, and in our opinion not only is it mere waste of time to resort to the use of these applications, but they are apt to set up injurious irritation. Voltolini's method of running a little sponge attached to a laryngeal probe up and down the larynx, by which process soft growths are supposed to be torn from their attachments, has not proved very satisfactory in our hands.

The only really satisfactory method of getting rid of the growths is to remove them by operation. In the great majority of cases this should be accomplished by the intra-laryngeal operation under the guidance of a laryngoscopic mirror held in the left hand, the right hand being free for manipulating the instruments. We need not enter into any detailed descriptions of the methods of procedure to be adopted; their technique can only be acquired by long and careful practice, and without this the intra-laryngeal removal of growths is attended with grave risks of serious injury to the healthy structures. The use of a 20 per cent solution of cocaine or eucaine hydrochlorate does away with the necessity for long and repeated introduction of instruments in order to inure the patient's larynx to the interference of foreign bodies. In our opinion, Mackenzie's cutting forceps is the most generally serviceable instrument, but in special cases others may be preferable: thus Dundas Grant's safety forceps are very well suited for growths on the free edge of the vocal cords about their middle thirds. In some cases the galvano-cautery, the laryngeal snare, or cutting curettes may be better adapted for dealing with the neoplasm; in fact the choice of instrument will depend almost as much on the tastes and habits of the operator as on the shape of the growth.

Often great difficulties have to be overcome before the growths are finally eradicated, and some cases even now baffle the most skilful operator for a long time; yet by patience and perseverance a very satisfactory result may be confidently anticipated in the overwhelming majority of cases.

Should the growth be very large, and should there be a risk of its impaction in the glottis, and of suffocation, prophylactic tracheotomy should be considered, even if removal of the tumour by intra-laryngeal operation may be fairly anticipated; or at any rate during the time of this peril the patient should be placed where tracheotomy could be performed in an emergency. Such measures, of course, are only required in very exceptional cases.

In dealing with multiple papilloma in young children we have some special difficulties to face, both in regard to diagnosis and treatment: in diagnosis from the obstacles to a satisfactory laryngoscopic examination, though there are surprising exceptions to this rule; and in treatment from the clouding of the mirror by mucus, even when a general anæsthetic is used. The ordinary intra-laryngeal method has succeeded in but very few of these cases; and thyrotomy, in addition to its added risks of permanent impairment of the voice, has given no immunity against their recurrence in a great many instances, in spite of removal of the growths apparently very thorough.

Lambert Lack has found it comparatively easy to obtain a view of the larynx in young children by passing the tip of the left forefinger into the right pyriform sinus and hooking forward the hyoid bone, and with it the epiglottis and base of the tongue; or instead of the finger a long tongue-depressor may be used, with the distal end bent down abruptly to the extent of half an inch.

Scanes Spicer, also, has recently introduced a method which combines general chloroform narcosis with frequently-repeated local moppings of the pharynx and larynx of the patient until all secretion is thereby arrested, when he finds it possible to examine the patient laryngoscopically, and, if necessary, to proceed at once with the removal of the new growths, should such be found. These methods certainly deserve further trial. The same may be said of the employment of autoscopy (see p. 704) for the purpose of detection and prompt removal of growth from the larynx of a small child.

In young children, if there be no respiratory embarrassment, removal of the growths may be deferred with advantage: first, because of the tendency to recurrence; and, secondly, of the special difficulties in operating. Should there be any dyspnœa, tracheotomy ought to be performed, and the removal of the growths themselves postponed to a later period of life, when the child may have gained self-control enough to allow the intra-laryngeal interference.

We do not hope for much help from intubation, which has been recommended under these circumstances in order to do away with the dyspnœa and to promote absorption of the new growths. In the first place, no authenticated case is known to us in which absorption of the growths has resulted from this method; and, secondly, there must be serious risk of detaching fragments, and of pushing them down into the lower air-passages.

When, from the peculiar nature of the case, external operation is necessary, there are two alternatives: (i.) Thyrotomy; (ii.) Subhyoid pharyngotomy. For subglottic growths, producing respiratory embarrassment, thyrotomy is sometimes unavoidable; but the cases which cannot be dealt with by the natural passages are very few; and it has justly been laid down as a rule that a radical external operation in a case of benign laryngeal growth ought never to be undertaken unless an experienced laryngologist has failed to remove it by intra-laryngeal methods.

Pachydermia Laryngis.—Singers' Nodes.—The term pachydermia laryngis was originally applied by Virchow to circumscribed or diffuse thickening of the epithelium and subepithelial tissue of the vocal cords and other parts of the larynx covered by pavement epithelium, and of the ventricular bands.

Causes.—The affection generally occurs in men between the ages of thirty-five and sixty. Amongst its immediate causes are chronic alcoholism and excessive tobacco-smoking; it is especially prone to occur in those who subject the voice to prolonged strain. In not a few cases, however, no definite cause can be assigned for its appearance.

Pathology.—In addition to the thickening and cornification of the epithelium, the subepithelial connective tissue is thickened and sends papilliform processes into the epithelial layer. Inflammatory round-cell infiltration appears, but there is always a distinct line of demarcation between the epithelium and the connective tissue. The local thickening is often surrounded by more or less diffuse congestion and inflammatory thickening. Virchow describes the cases due to syphilitic or tuberculous laryngeal disease as secondary or symptomatic forms of pachydermia; these varieties, however, need not be noticed here. Every degree of thickening may occur, from the slightest elevation, due to the heaping up of a few epithelial cells, to a well-defined lenticular tumid outgrowth a quarter of an inch or more in length.

Symptoms.—Often no symptoms are noticeable; but hoarseness and discomfort, slight pain, and considerable impairment in the compass, strength, and quality of the singing voice may be produced.

Objectively, the thickening is generally observed on the vocal processes, or interarytænoid fold, on one or both sides of the larynx. If bilateral, the wart-like growths are symmetrically placed, and, in the later stages, there is invariably a crateriform depression or pouch at the summit of one side into which fits a corresponding elevation on the other; thus apposition of the vocal cords is retained and the voice is preserved. This unilateral crateriform depression, as pointed out by Frankel, is probably the result of pressure by the opposite elevation, and not of the firmer fixation of the mucous membrane to the connective tissue at this spot, as Virchow believes; if the latter view were correct, the depression would not be invariably unilateral. Diffuse chronic laryngitis, chronic inflammation of the mucous membrane of the larynx, and even chronic adhesive perichondritis may coexist with the pachydermial affection, and sometimes render the diagnosis less easy.

Chorditis tuberosa, or "singers' nodule," or "teachers' node," is a clinical variety of pachydermia. A peculiar small poppy-seed-like growth appears on the upper surface and free border of one or both vocal cords, generally about the junction of the anterior third with the posterior two-thirds of its length. Possibly the tendency in them to occur at this particular spot may be that in singing there is a nodal point here which is subject to continual attrition. These nodules are the consequence of over-use or wrong use of the voice; they interfere particularly with the production of the notes of the upper register, and are most commonly seen in sopranos and tenors.

The nodes are merely local hypertrophies of the epithelium and subepithelial connective tissue of the vocal cord, and are usually very hard and consistent. If considerable in size, a small blood-vessel may often be seen coursing over the surface, and circumscribed hyperæmia of the immediate neighbourhood is frequently present.

The diagnosis rarely presents much difficulty unless the pachydermia be complicated by chronic laryngitis or perichondritis. The crateriform depression above referred to is pathognomonic of the affection, and, in our experience, the mobility of the vocal cords is unimpaired: impaired abduction of the vocal cords, however, has been described. Early malignant disease of the vocal cord may simulate pachydermia, but in this case impaired mobility of the vocal cord would almost certainly be present; and bilateral affection of the cords favours the diagnosis of pachydermia. In doubtful cases examination of a removed fragment may be possible; but only positive evidence of cancer would be of any value, and the failure to discover anything characteristic of malignant disease should have no weight in cases where the clinical appearances were indicative of malignancy.

A difficulty may arise in distinguishing between simple or idiopathic pachydermia and the epithelial thickenings and outgrowths that sometimes spring from syphilitic deposits; especially as these forms are but little affected by antisyphilitic treatment. Similarly tuberculous deposits in the interarytænoid fold may give rise to difficulty in diagnosis, if bacilli cannot be found in the sputum and if the pulmonary conditions are indefinite.

Prognosis.—The prognosis as regards life and function is invariably favourable; but the affection resists treatment and is very apt to recur.

Treatment.—In our experience the patient practically always gets well under prolonged vocal rest and the steady use of iodide of potassium; especially if any contributory causes, such as smoking and alcoholism, are corrected. Attempts at removal by operation are liable to set up perichondritis; but electrolysis, under cocaine, with bipolar instruments has been recommended by Chiari.

Malignant disease of the Larynx.—*Etiology.*—The causes of malignant growths in the larynx are as obscure as are the causes of malignant growths in other parts of the body. Heredity, excessive use of the voice, and long-continued local irritation are commonly held to have some influence in their production; but the experience of one of us (F. S.), who has had the opportunity of seeing an unusually large number of cases of malignant disease of the larynx, and has paid special attention to these factors, lends no support to these surmises. As a matter of fact, it is hardly ever possible to assign the cause of the occurrence of malignant disease of the larynx.

Men are certainly much more frequently affected than women, and the disease belongs especially to late adult life, being seldom met with before forty. The thirty years of life between forty and seventy supply the overwhelming proportion of all cases of malignant disease of the larynx coming under observation; and of these thirty years by far the largest place is taken by the decade between fifty and sixty. It must be stated, however, that a comparatively large number is met with in the decade from forty to fifty; that is to say, in that portion of life in which innocent growths also are not uncommon, and in which the differential diagnosis between benign and malignant growths, particularly in the earliest stages, is sometimes one of the greatest possible difficulty.

Pathology.—Both carcinoma and sarcoma occur in the larynx; and of these the former is met with far more frequently than is generally believed, while the latter are very rare. Carcinoma of the larynx is almost always either primary, or arises by direct extension from neighbouring structures; it almost never arises by metastasis or secondary infection. This immunity is owing to the arrangement of the lymphatics of the interior of the larynx, which are very richly developed, but form a network of their own without anastomosis with the lymphatics of neighbouring structures; they empty themselves into two small glands on each side, one beneath the greater cornu of the hyoid bone, the other at the side of the trachea. This peculiar arrangement of lymphatics is a point of the greatest clinical importance, for it explains, in the first place, why the larynx does not become affected secondarily in carcinoma of other parts of the body; and, secondly, why malignant disease occurring in the interior of the larynx tends to remain localised for a long time without affecting neighbouring lymphatic glands of the neck and other tissues: sometimes, indeed, secondary glandular enlargement may be absent to the very end. Consequently, following Krishaber, we shall subdivide cases of malignant disease of the larynx into *the extrinsic variety*, affecting the epiglottis, arytæno-epiglottidean folds, arytænoid regions, interarytænoid fold, and the posterior surface of the cricoid plate, and into the *intrinsic variety*, including the growths originating from the vocal cords, the ventricular bands, the ventricles of Morgagni, and the subglottic growths within the borders of the larynx proper.

In the great majority of cases the cancerous growths appear in the form of epithelioma; much more rarely we meet with medullary carcinoma and scirrhus.

Sarcoma occurs in the round-celled and spindle-celled forms as lymphosarcoma, myxo-sarcoma, fibro-sarcoma. The histological characters of the varieties of malignant growths in the larynx differ in no essential characters from malignant growths generally.

As regards the situation of the growth, intrinsic cases are met with more frequently than extrinsic. Amongst the extrinsic forms, malignant disease of the posterior surface of the cricoid cartilage seems to occur by far the most frequently; while in the intrinsic variety, so far as can be made out, malignant disease of the vocal cords heads the list by a long way. But in a very large proportion of cases the exact starting-point cannot be ascertained with certainty; only too often patients do not seek the advice of the specialist until the disease is already in an advanced stage. These statements are well exemplified by a series of 103 cases seen in private practice by one of us (F. S.). In 38 the growth was of the extrinsic variety, in 55 it was intrinsic; while in 10 it was mixed, that is, both extrinsic and intrinsic. Excluding these 10 the cases were distributed as follows:—

EXTRINSIC.	
Epiglottis	8
Arytæno-epiglottic ligament (probably)	5
Interarytænoid fold (probably)	6
Posterior surface of cricoid cartilage	19
Total	38

INTRINSIC.	
Vocal cords	15
Ventricular bands	3
Ventricle of Morgagni	2
Not to be made out with certainty	35
Total	55

Symptoms.—These vary greatly, not only in different stages of the disease but also with the situation of the growth; and while there is comparatively little difficulty in diagnosing the real nature of the affection when it has attained even a moderate degree, it is of the greatest importance from the therapeutical standpoint duly to recognise its earliest manifestations. Thus it is essential that careful attention should be paid to symptoms and to laryngoscopic aspects of the larynx that at first sight may appear almost trivial.

Hoarseness, in intrinsic cases, is nearly always the earliest and most frequent symptom. Its degree, even in the earliest stages when but a small tumefaction or projection from the vocal cord is to be seen, often is out of proportion to the size of the neoplasm. This is due to the infiltrating character of malignant growths, in consequence of which

DISEASES OF THE NOSE, PHARYNX, AND LARYNX

I.—DISEASES OF THE NOSE

RHINOSCOPY :
ACUTE RHINITIS :
CHRONIC HYPERTROPHIC RHINITIS :
CHRONIC ATROPHIC RHINITIS :
PURULENT RHINITIS :
MEMBRANOUS, ETC., RHINITIS :
EPISTAXIS :
TUBERCULOSIS :
LUPUS :
SYPHILIS :—F. de Havilland Hall.
NEW GROWTHS :
BONE AFFECTIONS :—Greville MacDonald.
RHINOSCLEROMA :
GLANDERS :—F. de Havilland Hall.
NEUROSES. Felix Semon and Watson Williams.
FOREIGN BODIES :
RHINOLITHS :
MAGGOTS :—F. de Havilland Hall.
DISEASES OF ACCESSORY SINUSES. Greville MacDonald.
NASO-PHARYNGEAL CATARRH :
TUBERCULOSIS }
SYPHILIS } OF NASO-PHARYNX :—F. de Havilland Hall.
ADENOID VEGETATIONS. Felix Semon and Watson Williams.

Rhinoscopy.—Anterior rhinoscopy is the name applied to the examination of the anterior nares, and posterior rhinoscopy to the examination of the naso-pharynx and posterior nares.

For rhinoscopy the same reflector and source of illumination are employed as for laryngoscopy. In examining the anterior nares various kinds of specula are used for dilating the nostril; the most convenient is Duplay's bivalve speculum. The examination of the nose is much facilitated by applying a 20 per cent solution of cocaine to the interior of the nostril, as in consequence of the astringent action of the drug on the mucous membrane a much better view is obtained of the posterior part of the nasal passages. The addition of resorcin to cocaine—in the proportion of 1 to 2—diminishes the toxic and increases the anæsthetic effect. In the methodical examination of the nose the condition of the mucous membrane and the presence and apparent source of any discharge should first be noted; then attention should be directed to the bony and cartilaginous framework of the nose, to deviations of the septum, and to any spurs and crests on it: finally, the presence of new growths and their points of origin should be recognised.

For the examination of the naso-pharynx and posterior nares a tongue depressor and a rhinoscope are necessary. Michel's instrument is the most convenient form of the latter. A cone of light should be thrown on the posterior wall of the pharynx by means of the laryngeal reflector, the tongue should then be depressed by a suitable depressor and the rhinoscope, the mirror having been first warmed, introduced behind the soft palate. When in position the trigger should be pressed so as to elevate the mirror. Three main difficulties are met with in posterior rhinoscopy: (i.) A hard palate which extends so far back that there is no room for the introduction of the mirror; (ii.) A broad and deep soft palate with a long uvula; (iii.) The instinctive drawing backwards and upwards of the soft palate on the introduction of the mirror. The first condition, which is fortunately rare, presents an insuperable obstacle to rhinoscopy; the second and third may be overcome by the use of a cocaine spray, and a little practice. Various hooks and snares have been devised for pulling the soft palate forward, but more will be accomplished by patience than by means of this kind.

The first thing to be recognised in posterior rhinoscopy is the septum, having identified this, the lower turbinals and sometimes the superior turbinal can be seen on either side, together with the *choanæ* or posterior openings of the nasal passages; then the mirror should be turned to the right and left in order to see the openings of the Eustachian tubes; finally, the mirror should be directed upwards so as to examine the vault of the pharynx. The appearances met with here vary very much. In children, a red irregular mass, constituting the so-called adenoid vegetations, is frequently to be seen; in adults, without an enlargement of the pharyngeal tonsil, the vaulted condition of the naso-pharynx may be distinguished.

In making a rhinoscopic examination it must be remembered that it is impossible to get a complete view of the whole of the posterior nares at the same time; segments only of the picture can be obtained, as the position of the mirror is shifted.

Acute Rhinitis.—Nasal catarrh and coryza are some of the names applied to an ordinary cold in the head. Here we have to do with an acute catarrhal inflammation of the nasal mucous membrane.

That the disease is of bacterial origin seems highly probable, but at present no proof to this effect is forthcoming. If acute rhinitis be due to bacteria, then exposure to cold and damp is a remoter cause, and the contagious nature of the disease is explicable. The symptoms associated with a cold in the head are so well known that it is quite unnecessary to mention them here.

In children, especially infants at the breast, acute rhinitis may be a serious affection. The infant, being unable to breathe through the nose, cannot take the breast; and if it be placed on its back the nasal obstruction may cause cyanosis and other symptoms of suffocation.

Treatment.—Persons who are subject to attacks of coryza may do much to prevent their recurrence by attention to the rules of hygiene. The clothing should be suitable to the season of the year, and never too thick. Exercise in the fresh air is most important, and a cold bath in the morning, followed by vigorous friction, is useful for all, except very young, old, or delicate persons. The diet should be simple, and over-eating is to be avoided. If the patient be anæmic, iron, arsenic, and cod-liver oil are the appropriate remedies. Attempts may be made to cut short an attack by taking ten grains of Dover's powder at night, full doses of the solution of acetate of ammonia, and hot drinks. The sulphate of atropine in doses of $\frac{1}{120}$ to $\frac{1}{60}$ of a grain has been found useful in many cases. After the more acute symptoms have subsided, quinine will usually be found of service.

Locally various antiseptic and sedative preparations have been recommended. Spraying the nostrils with menthol and eucalyptol dissolved in liquid paraffin is useful. A snuff composed of seventy-two parts of boric acid, twenty-five of salol, two of cocaine, and one of menthol, may be employed about every half-hour. The carbolised smelling-salts often give great relief. In cases of coryza in infants the nostrils may be kept clear by passing a small roll of blotting-paper into them. Liquid paraffin containing 2 per cent of cocaine can be applied to the nostrils with a paint brush, and will do much to promote the comfort of the infant.

Early treatment of nasal catarrh in children is most important. Any obstruction to free nasal respiration should be removed, and parts normally separate should not be allowed to touch one another.

Chronic Hypertrophic Rhinitis.—As a result of repeated attacks of acute rhinitis the nasal mucous membrane becomes thickened, and to this condition the term of chronic hypertrophic rhinitis is applied. Any obstruction to free nasal respiration, such as that offered by outgrowths from the septum, or deflections of it, increases the tendency to hypertrophic changes in the nasal mucous membrane. The irritation caused by the inhalation of dust, flour, and other substances suspended in the air also leads to similar changes. Various cardiac, pulmonary, and hepatic affections produce engorgement of the mucous membranes in general, including the nasal mucous membrane. Hypertrophic rhinitis is not infrequently found associated with adenoid vegetations and enlarged tonsils, and the tendency to these conditions seems to be hereditary. In addition to the changes usually met with in mucous membranes as the result of a chronic inflammatory process—namely, increase of the fibrous and lymphoid elements of the part, with more or less atrophy of the glandular structures—attention has of late been strongly directed to a permanent distension of the venous sinuses. This form of hypertrophy is especially marked at the posterior extremity of the inferior turbinated bodies, and has received the name of turbinal varix.

The symptoms of chronic hypertrophic rhinitis are almost entirely dependent on the nasal stenosis which it causes. The amount of visible obstruction affords no measure of the amount of discomfort to the patient. In neurotic patients a slight degree of stenosis produces symptoms out of all proportion to the obstruction.

The difficulty in breathing through the nose leads to mouth-breathing, and consequently to pharyngeal and laryngeal catarrh. The patient is constantly coughing and hawking to get rid of the viscid mucus which adheres, to the naso-pharyngeal, pharyngeal, and laryngeal mucous membrane. In some cases sneezing and a continual flow of mucus from the anterior nares are the chief troubles; in other instances headache, giddiness, and deafness due to implication of the accessory sinuses and Eustachian tubes. Mental depression, amounting even to melancholia, may result from hypertrophic rhinitis. At night for some obscure reason all the symptoms of stenosis are aggravated.

Chronic hypertrophic rhinitis can be distinguished from vaso-motor rhinitis by the application of a solution of cocaine, which in the latter affection causes the mucous membrane to contract, whereas in the former it has but little effect. New growths are usually more or less pedunculated; and, in any case, the growth is generally circumscribed. Bony and cartilaginous tumours may be excluded by their hardness. The appearance of a pale ashy gray or pink growth blocking up one or both choanæ, as seen by the aid of the rhinoscope, is very characteristic of enlargement of the posterior extremity of the inferior turbinal.

Treatment.—The line of treatment to be adopted depends to a certain extent upon the nature of the symptoms. If the patient is most troubled by the secretion of viscid mucus, which he has difficulty in getting rid of, various alkaline or mildly astringent sprays will be found useful. In some cases great relief is obtained by the use, night and morning, of one of the fluid paraffins in an oil atomiser. Menthol, eucalyptol, resorcin, or carbolic acid may be added to the paraffin.

Usually, however, some more radical treatment is requisite in order to reduce the bulk of the hypertrophied mucous membrane. Anteriorly this may be done by the use of the galvano-cautery, by incisions with a knife down to the bone, or by forming an eschar with chromic, nitric, or trichloracetic acid. If the tissue be of a polypoidal nature the anterior extremity of the inferior turbinal should be transfixed with a curved needle, and the galvano-caustic loop passed over the handle and point of the needle, and gradually tightened. Electrolysis has given excellent results in some cases. For hypertrophy of the posterior extremity of the turbinal it is advisable to use a wire-snare ecraseur, on account of the tendency to hæmorrhage from the dilated sinuses. The cold wire is also better in this locality on account of the proximity of the Eustachian tube, and of the risk of setting up otitis media by the use of the galvano-caustic loop. Dr. Greville MacDonald's nasal snare is a very convenient instrument. The operation should be performed slowly, a turn being given to the screw from time to time; if so done, there is hardly any bleeding. Should hæmorrhage occur, the injection of hot water will generally check it; if not, the nose may be plugged posteriorly. Some operators prefer the ring or draw-knife. In all operative procedures about the nose the greatest care should be taken to carry out strict antiseptic precautions. Some operators advise that the nose should be carefully sprayed with some disinfectant before it is treated. The application of cocaine is now universal, as it abolishes pain, and by constringing the mucous membrane allows a better view of the interior of the nose. After cauterisation or other operative interference in the nose, a pledget of cotton wool smeared with some antiseptic ointment should be introduced into the nostrils, and the patient warned against the risk of exposing himself to any septic influence.

The general treatment of cases of hypertrophic rhinitis requires a little consideration. A high, dry, and bracing locality has usually a beneficial effect, especially after the patient has had a course of treatment at a place like Ems. I have seen good results from a stay at Strathpeffer. Visceral engorgement must be treated with tonic aperients, such as the combination of the sulphates of iron and magnesium. The patient should be advised to take but little alcohol and to have regular exercise in the open air.

Chronic Atrophic Rhinitis.—Many authorities use the term ozæna as a synonym for chronic atrophic rhinitis; but this is incorrect, as ozæna (that is, a fœtid discharge from the nose) may occur independently of atrophic rhinitis, and there are cases of atrophic rhinitis without ozæna.

Etiology.—Chronic atrophic rhinitis begins in early life, and some authorities regard it as due to a congenital defect. The disease is not often recognised under the age of four or five years; it increases in severity towards puberty, and the majority of cases arise before the age of sixteen. Females are more frequently attacked than males, in the proportion of about seven to two.

It appears to be more common in anæmic patients and in those of phthisical parentage; but there is no general consensus of opinion on this point: some authors state that it usually occurs in persons who are otherwise perfectly healthy. Yet atrophic rhinitis frequently affects more than one member of the same family.

Morbid anatomy and pathology.—In some cases atrophic rhinitis is preceded by a hypertrophic stage, in which there are dilatation of the blood-vessels and emigration of leucocytes. Very soon the blood-vessels lose their tonicity, supply of blood to the part fails, and atrophic changes are the consequence. Many authors, however, hold the opinion that chronic atrophic rhinitis represents an atrophic process from the beginning, with sclerosis of the tissues and metamorphosis of the epithelium.

Bosworth is of opinion that atrophic rhinitis is almost invariably the result of the purulent rhinitis of children, and there is much to be said in its favour. By Zaufal the disease is regarded as due to a congenital defect, or to an arrest in the development of the turbinated bones. In atrophic rhinitis the turbinated bones are undoubtedly small; but this change is rather a part of the general atrophy of the structures of the nostrils than the cause of the disease.

Atrophic rhinitis is indeed the most common cause of ozæna, although cases of chronic atrophic rhinitis do occur in which ozæna is not present. Any condition which leads to a permanent dilatation of the cavity, as for instance the presence and removal of a nasal growth, may be the cause of ozæna. Michel regards chronic catarrh of the accessory sinuses as essential to the existence of ozæna; and Tissier lays especial stress upon a diseased process in the ethmoidal cells, or in one of the accessory sinuses, with necrosing osteitis, as the primary cause of ozæna.

The relation of micro-organisms to the production of ozæna is still undetermined. Loewenberg has described a micrococcus, resembling the pneumococcus, which he discovered in the mucous membrane, and he regards it as the cause of the condition. Hajek has detected in ozæna a short bacillus, occurring in the form of a diplococcus or in chains, which possesses the property of decomposing organic substances with the formation of a penetrating stink. Hajek has applied the name of *bacillus fœtidus* to this organism. When we have decided whether these micro-organisms are to be regarded as the cause or effect of the disease, the further difficulty will still remain of settling to which micro-organism the production of ozæna is to be assigned; for no one of them is found in all cases.

At the post-mortem examination of cases of atrophic rhinitis extreme atrophy of the mucous membrane and bony structures is found, and a fibroid degeneration of the soft parts: the ciliated epithelium is replaced by the non-ciliated variety. Krause regards fatty degeneration in the gland epithelium as an essential feature in the disease, and he attributes the sickening and rancid smell, so characteristic of it, to the decomposition of the fat and liberation of fatty acids.

Symptoms.—The patient usually complains of a sense of discomfort, and of obstruction in the nostrils; on blowing the nose violently masses of dry crust are expelled, together with a more or less fluid secretion.

Attempts have been made to divide atrophic rhinitis into two varieties—the dry and the moist; but there is no advantage in this, as in the same patient at one time crusts are found, and at another time the secretion is more liquid. The state of the atmosphere influences the nature of the discharge; in dry weather with east winds the discharge is dry, whereas in damp weather it is muco-purulent. A characteristic feature of the disease is the extreme fœtor of the discharge, which has a sickening, penetrating character; this when once perceived is readily recognised. Fortunately for the patient his sense of smell is usually destroyed early in the progress of the disease, so that he is unconscious of the horrible stench proceeding from his nostrils. As already mentioned, however, there may be no fœtid discharge.

Though the disease is not painful the nose is often very irritable, so that the patient picks or scratches the interior, and may thus cause excoriation of the mucous membrane and slight hæmorrhage. Such picking at the septum may lead to a perforation of the tissues already thinned by the disease.

Owing to the condition of the nasal mucous membrane, the air which passes over it in inspiration is not properly warmed, moistened, or filtered; thus pharyngeal and laryngeal catarrh are frequently met with in patients suffering from atrophic rhinitis; in some cases crusts form in the larynx and trachea—" tracheal ozæna "—and cause fœtor of the breat even after the nostrils have been thoroughly disinfected.

By extension of the disease to the Eustachian tube, acute and chroni catarrh of the middle ear and tinnitus sometimes arise. Ulcer of th cornea with hypopyon and conjunctival catarrh and various refle symptoms are observed occasionally.

The aspect of the patient suffering from chronic atrophic rhinitis i characteristic; the nose is broad and depressed at the bridge, giving ris to the condition called saddle-back, and the tip is turned up, showing th dilated nostrils. On anterior rhinoscopy the nostrils will be found full o dry crusts composed of inspissated muco-pus and micro-organisms, an having an abominable stench. On removal of these the nasal passages wil be found unusually capacious, so that it may be possible to see the posterio wall of the pharynx. The mucous membrane of the nose is generall pale, but it may sometimes be slightly reddened. Ulceration is rare, bu a little bleeding may follow the detachment of the crusts. Should ther be necrosis of bone or cartilage the case is not one of atrophic rhinitis. Atrophy of the turbinated bodies, however, is a marked feature of the disease.

On posterior rhinoscopy, after the removal of the crusts, a similar condition of atrophy will be found in the naso-pharynx. The pharynx is dry or glistening, or covered with mucus blackened by soot and other impurities of the air. Crusts may also be seen in the larynx.

Diagnosis.—The characteristic stench issuing from the nostrils, the crusts which block them, and the dilated state of the nostrils seen after the removal of the crusts render the recognition of the disease easy. Moreover, the disease affects both nostrils, whereas the presence of foreign bodies causes a unilateral discharge; and in these cases a careful rhinoscopic examination ought to clear up any doubt. Syphilitic disease of the nose leads to ulceration and necrosis of the subjacent bone, but neither of these conditions is present in atrophic rhinitis. Suppuration of one antrum should be readily distinguished; but if both antrums were affected, causing a discharge from both nostrils, there might be some difficulty in diagnosis. In affections of the antrum the patient complains of the smell more than his friends do, the discharge is purulent, and its amount is increased by lowering the head; moreover, the test of transillumination with the electric light will aid in the diagnosis.

Prognosis.—Chronic atrophic rhinitis is not a disease attended with any danger to life, but the amount of annoyance it causes is at times sufficient to make life hardly endurable, and it may render the patient unfit to earn his livelihood. Though the cure of a marked case of atrophic rhinitis is not to be expected, by careful and prolonged treatment the disease can be deprived of its worst features. The disease reaches its climax about the age of twenty, is less troublesome in middle life, and is hardly noticed in old age. The symptoms, especially the stench, are always worst at the catamenial period.

Treatment.—Such is the difficulty of curing cases of atrophic rhinitis, that it is extremely important that any conditions which seem to stand in a causal relation to this disease should be promptly met. Hence the purulent rhinitis of children should receive early and appropriate treatment; adenoid vegetations and enlarged tonsils, which so frequently lead to persistent nasal catarrh, should be removed, and attention should be directed to the condition of the accessory sinuses. At the same time the general health of the patient should be improved as much as possible; anæmia, debility, or a tuberculous tendency must be combated by fresh air, good food, and the administration of iron, arsenic, and cod-liver oil.

Whatever plan of local treatment be adopted, the essential part of it is the thorough cleansing and disinfecting of the nasal cavities. This is most conveniently effected by spraying the nostrils with a warm alkaline solution; 5 grains of borax and the same amount of bicarbonate of sodium in an ounce of water answers well. A 10 per cent solution of hydrogen is highly recommended for the same purpose, and it has the additional advantage of acting as a disinfectant. If the crusts are very hard, it may be necessary to remove them with the nasal forceps. When the nostrils have once been thoroughly cleansed the patient should be instructed to use the spray two or three times a day, or as often as is necessary to keep the nose sweet. After a time various astringents and antiseptics may be tried; for instance, 2 to 5 grains of resorcin, sulphate of zinc, or alum respectively, in an ounce of water; or 6 minims of the liquor potassii permanganatis in an ounce of water: or the nose may be swabbed out with a solution of nitrate of silver—5 to 10 grains to the ounce—dissolved in a 20 per cent solution of nitrate of cocaine. In some cases, after the nose has been sprayed, the insufflation of iodoform, iodol, aristol, or boric acid will give good results. An excellent plan of treatment is, after thorough cleansing, to spray the nose with one of the liquid paraffins, for instance, paroleine containing in solution some antiseptic such as menthol, thymol, or eucalyptol. The application of a solution of trichloracetic acid (5 to 20 parts in 1000) by means of cotton wool on a suitable holder, quickly and safely removes the smell of ozæna

In intractable cases Gottstein's tampon is very serviceable. To obtain the best effect the plug of cotton wool should be in contact with the whole of the interior of the nostril. In some cases the plug acts more powerfully if moistened with glycerine. The action of the plug is to stimulate the nasal mucous membrane, and, by causing an increased secretion, to prevent the formation of the crusts. Massage, vibration-massage, electrolysis, and the constant current are said to give excellent results in suitable cases.

Purulent Rhinitis.—A purulent discharge from the nostrils occurs as the result of many different causes. In the first place, it may be due to empyema of one of the accessory sinuses; this of course must be distinguished from purulent rhinitis. The presence of adenoid vegetations, again, is a very common cause of nasal suppuration; restriction of pus to the floor of the nose and to the posterior wall of the pharynx is pathognomonic of this variety. In the acute specific infectious diseases—scarlet fever, measles, small-pox—a purulent nasal secretion is frequently observed; as also in cases of glanders, tuberculosis, and syphilis of the nose. In addition to these causes there is also a condition to which the name purulent rhinitis is more correctly applied. A purulent rhinitis is occasionally seen in the newly-born infant, analogous to the purulent ophthalmia of infants and dependent on gonococci of maternal origin. This variety is seen immediately after birth, is purulent from the outset, and soon leads to excoriation of the upper lip as well as to painful swelling of the whole nose. Adults suffering from gonorrhœa may infect themselves or others. Children of a strumous diathesis, or otherwise in delicate health, are apt to suffer from nasal catarrh which frequently becomes purulent. Bosworth lays great stress on the purulent rhinitis of children, as he maintains that it may be the starting-point of atrophic rhinitis.

In addition to the causes already enumerated a purulent discharge from the nose may be due to the presence of rhinoliths, foreign bodies, polypi, and other new growths. The change seen in purulent rhinitis is that met with in suppurative inflammation of other mucous surfaces; namely, hyperæmia, at first with a mucous secretion which soon becomes muco-purulent: then, as rapid cell-proliferation takes place, the discharge becomes puriform, and no longer yields mucin. In infants the swelling of the mucous membrane may lead to nasal stenosis, and interfere with breathing and sucking. In children and adults the yellowish purulent discharge is the characteristic symptom.

The *diagnosis* must depend upon a careful examination of the nose and its accessory sinuses, with attention to any collateral symptoms.

The *treatment* must depend upon removal of the cause if possible. Hence the necessity for a careful examination of the nose and the treatment of polypi, rhinoliths, foreign bodies, and other causes of irritation. When this has been effected, various sprays—alkaline, antiseptic, or slightly astringent—may be employed. In children of a "strumous" tendency attention to the general health is most important.

Bearing in mind the possibility that purulent rhinitis may represent the first stage of atrophic rhinitis, every endeavour should be made to arrest the disease when it is still in a curable form.

Membranous, Fibrinous, or Croupous Rhinitis.—Under this head are included cases in which a membranous exudation forms on the surface of the nasal mucous membrane. In the majority of cases the disease is the result of diphtheritic infection, and in some the general symptoms are so slight that the true nature of the disease is likely to be overlooked. It is, therefore, only after a careful bacteriological investigation has been made, with a negative result, that the possibility of any cause other than diphtheria should be admitted. Until such examination has been made the patient should be isolated. In the non-diphtheritic cases various micro-organisms have been detected in the exudations; such as a coccus resembling the staphylococcus pyogenes aureus, but differing from it by its extraordinarily quick growth, and by the duration of its power of infection: the streptococcus aureus and the pneumococcus are also found.

Membranous rhinitis occasionally occurs in the new-born infant, usually in connection with septicæmia in the mother.

The application of the galvano-cautery to the nasal mucous membrane is sometimes followed by the formation of a false membrane, which, however, is limited to the cauterised surface. The exudation in simple membranous rhinitis resembles that of diphtheria; it has a grayish white colour, it is more or less firmly adherent to the subjacent mucous membrane, and on attempts to remove it a bleeding surface is left. In the non-diphtheritic cases the attack begins like an ordinary cold, the nose becomes blocked, and frontal headache may be a prominent symptom. The nature of the disease is only recognised by the detection of shreds of membrane in the secretion from the nostrils, or by making a rhinoscopic examination. A case has been recorded in which several recurrences took place. The slight and transient disturbance of the general system, the absence of glandular swelling, of membrane on the pharynx and nasopharynx, and of albuminuria and of secondary paralysis, together with the absence of contagious properties, distinguish simple membranous rhinitis from nasal diphtheria. The result of a bacteriological examination, and the fact that membranous rhinitis occurs sporadically, are of diagnostic importance. Attempts may be made to keep the nasal passage patent by the use of alkaline and antiseptic sprays. Painting the affected surface with a mixture of 5 grains of papain and 5 minims of lactic acid in a drachm of water will facilitate the separation of the membrane. The insufflation of iodoform, after the nasal passages have been sprayed with an antiseptic solution, has given good results. It is not advisable to remove the membrane forcibly, as under these circumstances it is apt to recur.

Epistaxis.—In cases of bleeding from the nose it is necessary to remember that the source of the blood may be at a distance, the nostrils merely serving as channels; or the blood may come from the nose itself. It is with the latter form of hæmorrhage that we have to do. The causes of epistaxis may be arranged according as the local or constitutional element plays the most important part in the hæmorrhage. The chief local causes are the various forms of rhinitis, tuberculosis, and syphilis of the nose; and the presence of new growths, especially those of a malignant nature. Leeches, worms, and maggots sometimes give rise to epistaxis. The most common local cause, however, is mechanical violence. In connection with the local origin of epistaxis, it should be borne in mind that in a large number of cases the blood comes from a spot on the anterior part of the septum; and from the frequency with which this connection is found to exist, this spot has come to be designated as the *site of predilection* of nasal hæmorrhage. In some cases the spot on the septum from which the bleeding comes can be recognised by varicose condition of the vessels, or there may be a small patch of erosion or ulceration; in other cases the mucous membrane is soft and spongy. The characteristic feature, however, is that on gently rubbing the part with a smooth sound bleeding occurs.

Among the constitutional causes which give rise to epistaxis are changes in the vascular system, as in Bright's disease, atheroma, and valvular disease of the heart. In lung affections (especially in emphysema and bronchitis) and in whooping-cough there is a tendency to nose-bleeding. Cirrhosis of the liver is frequently accompanied by the same symptom. In diseases attended with alterations in the composition of the blood—such as purpura, scurvy, chlorosis, anæmia, pernicious anæmia, leukæmia, and hæmophilia—epistaxis is a common symptom. Epistaxis is met with in all the acute infective diseases, especially in enteric fever. It may occur in the prodromal stage of measles, varicella, typhus fever, erysipelas, and, less frequently, in scarlet fever; but when it occurs at the end of the latter disease, it is to be referred rather to the kidney affection than to the fever. Epistaxis is not infrequent in diphtheria, even when the diphtheritic process is not localised in the nose.

In the recent influenza epidemic many cases of epistaxis have been noted, in most instances due to the catarrh accompanying this disease, but in some cases a special hæmorrhagic tendency seems to have arisen during the attack. Epistaxis occasionally follows the administration of drugs, such as phosphorus, salicylate of sodium, and chloralamide. Rarefied air, as in ballooning and mountaineering, and extremes of heat and cold sometimes cause nose-bleeding. Finally, epistaxis has been described as vicarious to the menstrual flow.

Epistaxis is rare in the newly-born, and occurs extremely seldom in the suckling; from the second year of life it begins to increase in frequency, and attains its maximum about the period of puberty; in adult life it is somewhat rare, but the tendency may again manifest itself in old age, as degenerative changes take place in the vessels. Epistaxis is more common in the male than in the female sex.

The amount of hæmorrhage in cases of epistaxis varies from a few drops up to several pints. The attacks may recur daily for many weeks, and then cease entirely for a considerable time; or there may be frequent attacks of slight hæmorrhage persisting for years; or, lastly, the attacks may be infrequent, but very severe. Epistaxis is sometimes preceded by headache, and relief follows loss of blood; in other cases, especially when the hæmorrhage has been large, headache may follow the attack. When the epistaxis depends on a lesion of the septum the blood usually comes from one nostril only. In hæmorrhage from the posterior part of the nares the blood, trickling down the pharynx, may excite cough and give rise to the suspicion of hæmoptysis. On the other hand, as I have said, blood may pour from the nostrils though its source may be quite remote, as in fracture of the base of the skull.

In the majority of cases epistaxis ceases spontaneously, and the individual is often the better for the loss of blood; occasionally, however, the loss may be excessive, and death has been recorded as the result of it. In hæmorrhage due to nasal diseases, with the exception of malignant new formations, a good prognosis may be given. In old people with degenerated vessels, and in cases of granular kidney, the occurrence of epistaxis requires a guarded prognosis, as one of the cerebral vessels may be the next to give way. In the presence of head symptoms the history of epistaxis is in favour of cerebral hæmorrhage. In diseases due to altered blood states epistaxis is always a grave symptom, and not infrequently the cause of death. In diphtheria the occurrence of epistaxis is an unfavourable sign, indicating probably that the membrane has spread to the nasal fossæ; in enteric fever, on the contrary, it often seems to give relief.

Treatment.—In a considerable number of cases, especially in young people, nose-bleeding seems to be an effort of nature to relieve plethora: no active treatment is required. It will suffice to keep the patient quiet, sitting up with the head somewhat forward, so that the blood may trickle down the anterior nares; anything which constricts the neck should be removed, the head should be kept cool and the feet warm. If the bleeding continue, and it is considered advisable to stop it, the patient should be told to raise his arms above his head; an ice-bag may be applied to the cervical spine, or the feet and legs placed in water as hot as can be borne. Should these measures fail, plugging the nose anteriorly will usually arrest the flow.

The most convenient plan is first to insufflate the nose with iodoform by means of Kabierski's insufflator; then to introduce a Duplay's speculum, and pass a long strip of iodoform gauze up through the speculum. In cases in which it is known from previous experience that the hæmorrhage comes from the septum, a small plug of iodoform gauze introduced within the nostril, and compression of the nose externally between the thumb and fore-finger, is generally sufficient.

Instead of plugging the nose with lint or gauze the instrument designed by Dr. Cooper Rose may be employed. This consists of an india-rubber bag, connected with a tube, which is provided with a stop-cock. The bag is introduced into the nose in a flaccid state, and is then inflated by the tube.

In cases of recurrent hæmorrhage from the septum, the most effective cure is to apply the galvano-cautery at a dull red heat to the source of hæmorrhage, after the previous application of a 20 per cent solution of cocaine. After cauterisation a small pledget of cotton wool smeared over with carbolised vaseline or boric acid ointment should be placed in the nostril. If plugging the nose anteriorly fail to stop the bleeding, the method of posterior plugging must be employed. Inasmuch, however, as otitis media and other dangers have resulted from its employment, it is desirable not to have recourse to it unnecessarily. The best instrument for carrying out the posterior tamponage is Bellocq's canula. The canula, which contains a watch-spring fixed to a stylet, is passed into the nostril. By turning a screw the watch-spring runs down the canula, and protrudes into the mouth. The piece of string which is tied to the end of the spring can then be seized and attached to a pledget of lint of sufficient size to occlude the posterior naris. The canula is now withdrawn through the nostril, carrying with it one end of the piece of string, and this is tied to the other end which protrudes from the mouth. After the nostril has been plugged posteriorly it may be necessary also to plug the nose anteriorly. This should be done in the manner already indicated. It is not advisable to leave the plug in the nostril more than thirty-six or forty-eight hours. The posterior plug may be removed by making traction on the string coming through the mouth. If there be any difficulty in withdrawing the plug the nostril must be irrigated with a warm alkaline solution.

In the absence of Bellocq's canula a gum-elastic catheter, or a piece of silver wire, doubled so as to form a loop sixteen inches long, may be employed for drawing the string through the nose.

Instead of plugging, various styptic solutions have been used for spraying the nose; among these may be mentioned vinegar, lemon juice, and tincture of hamamelis.

Water at a temperature of 110° to 120° F., or even higher, has been found extremely useful in arresting hæmorrhage from the nose.

Lastly, in cases of epistaxis due to liver disease speedy cure has been effected by the application of blisters to the right hypochondrium.

Tuberculosis of the Nose.—Tuberculous disease of the nose is almost invariably secondary to tuberculosis of other organs, especially of the lungs and larynx; but cases have been recorded in which tumours containing tubercle bacilli have been discovered in the nose when the lungs and other organs seemed healthy. This may well be so, as tubercle bacilli are to be found in the nostrils of healthy persons who are associated with consumptives, as in a hospital. It is possible, also, that tuberculosis of the nose may be set up by the introduction of infectious material by the finger, or by using the pocket-handkerchief of a phthisical patient. In the majority of cases the onset of the ulceration is to be attributed to local infection.

Chronic catarrh, the formation of crusts with a dry condition of the mucous membrane, fissures and abrasions of the epithelium produced by picking the nose, offer a footing to the tubercle bacilli, which, if the soil be suitable, multiply and give rise to the characteristic lesions.

Tuberculosis of the nose occurs in the form of either a tumour or an ulcer. No strict line of demarcation can be drawn between tumour and ulcer, since the former may become ulcerated; or the two may coexist; or nodules may arise on the margin of an ulcer in process of healing.

In forty-eight cases out of ninety, collected by Heryng, ulcers were present; and in forty-two tumours were seen. In the majority of cases the tumours are chronic and local, interfering with the general health little, if at all; on the other hand, ulcers occur for the most part secondarily. Bosworth describes tuberculous tumours as springing from one of the turbinals, and resembling a small papillomatous growth, but flatter, more regular, and of a reddish gray colour. Usually, however, the tumours occur as irregular red growths on the septum, which readily bleed when touched. They may attain the size of a hazel nut. The cartilaginous septum is the favourite seat of the ulcer, more rarely it is seated on the membranous part; the ulceration may extend to the alæ nasi, and even to the upper lip, and may lead to perforation of the septum. The edges are sometimes thickened and everted, but in other cases they are clean cut. The surface of the ulcer is of a grayish colour, and is covered either by a muco-purulent secretion or by a crust. Tubercle bacilli may be absent from the superficial layer whilst they are abundantly present deeper down.

Symptoms.—Pain, hæmorrhage, and nasal obstruction are the most prominent symptoms. In some cases the nose is swollen. There is usually an increase of the nasal secretion, which is sometimes offensive and may contain blood. Tuberculous disease of the nose usually runs a much more chronic course than a similar condition of the tongue or larynx, as the nose is not subject to the constant movement and irritation of the two latter organs.

Diagnosis.—Tuberculosis of the nose must be distinguished from lupus, syphilis, glanders, and the chronic eczema of the introitus nasi met with in strumous children. If the affection is confined to the nose it is almost impossible in some cases to exclude lupus; usually, however, to aid in diagnosis, there are the characteristic growths on the skin and mucous surfaces, and the tendency of lupus to improve and then to relapse. The absence of tubercle bacilli and the success of an anti-syphilitic treatment speedily clear up any doubt as to syphilis. Eczema is more superficial and usually involves the upper lip also. Tuberculous tumours of the nose must be distinguished from other tumours found in this region, such as sarcoma, fibroma, and the like.

Treatment.—As in all tuberculous affections, the general health of the patient must be maintained by good food, fresh air, and tonics. The most successful local treatment is to curette, after previous cocainisation, and to rub in lactic acid. Even though the treatment be vigorously carried out, relapses are frequently observed. For small ulcers the galvano-cautery may be employed, but the results are not so satisfactory as those of the lactic acid treatment. If operative treatment be deemed unadvisable, the nose should be cleaned with an alkaline solution, and then insufflated with iodoform, or sprayed with a 5 per cent solution of menthol in fluid paraffin.

Lupus of the Nose.—In the majority of cases lupus affecting the nasal passages is an extension of the disease from the face. If the nose were systematically examined in all cases of facial lupus many more cases of intra-nasal lupus would be reported. In rare instances the nasal mucous membrane is the primary seat of the disease [*vide* art. "Lupus" in a later volume].

Symptoms.—The patient's attention is usually first attracted by the formation of crusts and a feeling of irritation in the nostril; occasionally complaint is made of pain. The thickening of the mucous membrane and the crusting cause more or less nasal stenosis. There is but little discharge, and this is usually free from odour, unless the crusts have been retained in the nose sufficiently long to decompose. After spraying the nostrils in order to remove the crusts, the damage wrought by lupus may be recognised. In some cases ulceration is the most marked feature of the disease; in others the formation of nodules is the chief feature. Ulceration as a rule begins at the orifice of the nose, and the septum is attacked early. Perforation of the septum is accelerated by picking the nose. The ulceration may heal, or it may extend up to the edge of the vomer; the bone itself is attacked in exceptional cases only. The nodules seen in the nostrils resemble those met with on other mucous surfaces.

Diagnosis.—It is almost impossible to distinguish between some cases of chronic tuberculosis of the nostrils and lupus; indeed, if the view be correct that the latter is due to an attenuated tuberculosis, it can be readily understood that there is no line of demarcation between the two. Lupus of the nose is most likely to be confounded with syphilis; the latter runs a more rapid course, and attacks bone, whereas lupus usually spares bone. The absence of response to an anti-syphilitic treatment is a strong point in excluding syphilis. The soft, granular, irregular surface and opaque pale colour of the lupus nodules distinguish them from polypi. The recognition of lupus nodules on the external skin, and the microscopical examination of a portion of the growth, will confirm the diagnosis.

Prognosis.—Lupus usually runs a chronic course, and does not lead to a fatal termination. In one case, however, the septum was destroyed, and the sphenoid bone eroded; death took place from basic meningitis.

Treatment.—Local treatment must be carried out actively. Any outgrowths must be removed by the cold or galvano-caustic loop, and the cautery applied to the base. Some operators prefer the sharp spoon, followed by the application of chromic acid. Lactic acid answers well in the less severe forms. The local application of cold in the shape of an ice-bag to the nose has been successfully employed, the bag being placed on the nose for three hours, night and morning.

Should the case be too far advanced for any radical treatment, the nose should be sprayed with a simple alkaline solution to remove the crusts, and then a 5 per cent solution of menthol should be sprayed up the nostril with an oil atomiser.

Cod-liver oil, syrup of the iodide of iron, and arsenic are the internal remedies that promise the best results. Some of the lupus patients treated by tuberculin were permanently benefited; and it is possible that in properly selected cases there may still be a future for this remedy.

Syphilis of the Nasal Mucous Membrane.—Syphilis in all its forms —primary, secondary, tertiary, and inherited—may attack the nose.

Primary chancre of the nose is comparatively rare, nevertheless thirty-seven cases have been put on record up to the year 1894. Between 3 and 4 per cent of the cases of extra-genital syphilis belong to this category. The virus is usually conveyed to the nose accidentally; but cases of direct transference by the genital organ have been reported. The site of the chancre is most frequently at the orifice of the nose, and the surrounding parts have an erysipelatous appearance. The submaxillary glands are enlarged and tender. Primary syphilis of the nasopharynx has been met with in fourteen patients. In every case infection was conveyed by the Eustachian catheter.

In the absence of history a chancre in the nose would give rise to much difficulty in diagnosis before the supervention of secondary symptoms. It would most probably be mistaken for a sarcoma, but from this it may be distinguished by its tendency to bleed, by the small amount of swelling compared with the ulceration, and by the early enlargement of the submaxillary glands on the corresponding side. The orifice of the nose is the part usually attacked in the secondary stage, and, as on other mucous surfaces, the affection may assume a catarrhal, erythematous, or superficial ulcerative form. Condylomas have also been seen in the nose.

In the tertiary stage the nose is frequently and often severely affected. The disease usually begins as a gumma, though this stage may be overlooked, and the patient may not present himself until ulceration has occurred. In some cases ulceration takes place without the previous formation of a gumma. The damage wrought by tertiary syphilis in the nose is at times very great; there may be complete destruction of the contents of the nasal cavities, the antrum being thrown open on both sides. Perforation of the septum is a very common result of syphilis; the syphilitic affection differs from simple perforation in that the bone is attacked in the former, consequently a much greater destruction may occur; the ulcers are longitudinal, and the margins of the ulcer are thickened. As a result of cicatricial contraction of the connective tissue which binds the cutaneous and cartilaginous structures to the nasal bones, the so-called "saddle-back" nose may be formed. It is important to bear in mind that a similar condition may be brought about by phlegmonous inflammation of the nose without syphilis. In inherited syphilis it is very common to meet with a catarrhal condition of the nares giving rise to "snuffles." Inasmuch as ulceration at the angle of the mouth, a rash about the body, and condylomas usually occur at the same time, the diagnosis is easy. Later, especially about the period of puberty, the manifestations of inherited syphilis are such as are seen in the tertiary form of acquired syphilis.

Treatment.—Under the usual treatment for syphilis the swelling caused by the primary sore in the nose rapidly disappears, and leaves no traces except some scarring.

For secondary syphilis of the nose the usual constitutional treatment is required, with some simple alkaline solution to spray the nose, followed by insufflation of iodoform, or the application of dilute citrine ointment.

In tertiary syphilitic disease of the nose large doses of iodide of potassium are needed; and in some cases the inunction of mercurial ointment will accelerate the cure. The nostrils should be kept clean by spraying them with warm antiseptic solutions. If necrosis takes place, and the necrosed bone do not separate spontaneously, it may be necessary to remove it by forceps. When sequestra are seated above the middle meatus great care is needed in attempts at removal. The insufflation of iodoform will check the offensive odour and promote healing. In infants suffering from the coryza of inherited syphilis it is most important, in addition to constitutional treatment, to keep the nostrils open; this can be effected by spraying them with an antiseptic solution, and then applying dilute citrine ointment, or a 10 per cent solution of menthol in fluid paraffin.—F. DE H. H.

The new growths of the nasal cavities.—*Mucous Polypus.*—The production of polypus is either dependent upon, or actually consists in a more or less circumscribed inflammation of the mucous surface from which it springs. Where the growth is attended by suppuration the initial factor is probably an epithelial necrosis. As an immediate consequence of such an accident we find granulation tissue covering the ulcerating surface. The longer cicatrisation is delayed the larger these granulations become; and, being perpetually bathed in mucus, they absorb moisture, become œdematous in fact, and thus acquire an increasing tendency to fungate. This process is precisely that of an ordinary ulcerated surface where granulations are proliferating freely. If such an ulcer be bathed constantly in water the granulations become watery, pale, and flabby, and are scarcely to be distinguished histologically from many a specimen of simple mucous polypus.

As this incipient polypus grows older its structure becomes modified, owing to the production of a fibrous element. The growth becomes more prominent and the blood-vessels more developed, especially towards the base, where the fibrous element grows firmer and contracts the surrounding tissue; thus gradually a pedicle is produced containing fully-developed vessels which ramify in the peripheral and more œdematous tissue. Usually the structure ultimately becomes quite distinct from the surrounding surface from which it springs, although very often the mucous membrane in the immediate neighbourhood is in a condition of pronounced hyperplasia. As this granulation polypus increases in size we find, curiously enough, that the epithelium tends to creep over it from the base; and it is in this way that these growths are often found completely covered with ciliated epithelium. Precisely the same thing occurs in the ear where the similar so-called "polypus" admittedly consists originally of granulation tissue. In the tympanum such formations invariably are or have been associated with carious bone, a fact conclusively proving their inflammatory origin; yet even the epithelium of the tympanum creeps over these granulations, and covers them more or less completely with columnar ciliated cells.

Rindfleisch has described a fine reticular formation in the ordinary fungating granulation; and in the polypus we may find, associated with such reticulum, round cells which become larger and fusiform in various places, and are gradually converted into fibrous tissue. At an equal rate with the increase of reticulum the tendency to absorb water becomes more pronounced. Amid this increasingly coarse reticulum we find, in different parts, various quantities of cells of diverse shape and size; varying, that is to say, from the small granulation to the long fusiform cell, which probably produces the fibrous element. Such I believe to be the essential structure of mucous polypus.

While admitting that pathologists commonly describe polypus of the nose as either myxoma or adenoma, yet for my part, although I have examined some hundreds of specimens, I have never succeeded in finding a true myxoma cell. In the younger growths we may find a cell apparently branched at the points where the fine reticular fibres cross one another; yet an unmistakable myxoma cell I have never seen.

But although, clinically speaking, the initial inflammatory attack which results in polypus is often accompanied by suppuration, yet probably there is another method, possibly more frequent, in which these growths originate. A succession of acute attacks of cold in the head may gradually induce a chronic infiltration, weakening and thickening of a certain area of mucous membrane; the fibrous elements, becoming softened and granular, gradually disappear into mucous fluid which steadily increases in the interspaces. New cells are produced which, accumulating into clusters, ultimately produce a definite projection above the surface; and this granuloma may gradually pass through all the changes of fungating granulation tissue till a structure recognised as polypus is produced. In such case there need have been no loss of continuity in the epithelial surface.

Clinically, as I have said, we are perfectly familiar with the two different modes of formation; and, even if true myxomatous tissue occur occasionally in polypi, the fact does not militate in any way against my view of the inflammatory origin of such growths. For, as I have pointed out upon the authority of Rindfleisch, ordinary fungous granulations may contain a quantity of well-formed mucous tissue, presenting a pale pink, watery appearance, sometimes even yellow and jelly-like. Virchow, moreover, teaches us that mucin is a common product in irritated connective tissue, and that thus it must be admitted as a product of inflammation.

In cases where the initial inflammatory attack is of sufficient intensity to produce molecular necrosis of the mucous membrane, where, moreover, the tendency to heal is not strong enough even to produce a polypus, the ulceration may extend to the muco-periosteum and expose the subjacent bone. In such a way we may have masses of granulation tissue, well-formed polypi, and carious bone coexisting side by side; and where such a process takes place within any of the accessory cavities we then find abscess and other consequences attendant upon the retention of pus. But these points will be considered in a subsequent section.

Very frequently a portion of mucous membrane, especially when depending from the free border of the middle turbinal, presents such an appearance as makes one doubtful whether it should be considered as a diffuse polypus or rather as a mass of hyperplasia; nor will the microscope materially assist us in drawing the distinction. And if such a fragment do not appear sufficiently translucent to justify its being considered as polypus, we may, by soaking for a few minutes in water, so increase its size as to give it microscopically every characteristic of ordinary polypus tissue.

The description of the ordinary mucous polypus just mentioned does not account for the classification generally given by surgeons. We are told that the benign mucous polypus consists, as I have already remarked, either of myxoma or adenoma. The former misapprehension I have attempted to explain; but the other is less easy to comprehend, seeing that the growths for which the name polypus is now reserved by rhinologists never present any glandular structure, except, indeed, in cases in which the neoplasm consists rather of an œdematous hypertrophy of a widely-attached piece of mucous membrane. The fact is that the surgeon has habitually confounded with polypus those curious lobulated or cauliflower-like growths which consist entirely in a hyperplasia of the mucous membrane covering the erectile tissue more especially developed over the inferior turbinals. In such growths the normal mucous glands are often largely increased in size and number, and one readily realises how the name adenoma was applied to them. But, according to usual observance, the discussion of these growths belongs rather to the domain of chronic hypertrophic rhinitis, although there is no good reason for discussing polypi as new growths if the former are not to be similarly considered.

Clinical aspects.—On several occasions I have actually watched the inception of a polypus in an attack of acute inflammation; that is to say in cases where I knew that no suspicion of such growths had previously existed. The patient is seized with more or less severe pain, generally referred to the supraorbital region; while the intensity of the swelling and the obstruction to breathing are altogether out of proportion to the degree of inflammation on the opposite side. The acuteness of the pain probably points to inflammatory tension deeper than the mucous surface, that is to say in the muco-periosteum, or perhaps in an ethmoidal cell. After two or three days of such pain I have seen a polypus appear in the middle meatus, perfectly translucent, pale pink in colour, and sharply defined. But the more ordinary course is for the patient, after complaining of a constant succession of colds in the head, to find that his nose is becoming persistently obstructed. He tells us he is always worse in damp weather, he walks and sleeps with his mouth open, his eyes become watery and bloodshot, and his nose frequently widens across the bridge; unable to obtain any satisfaction from blowing his nose, he is perpetually wiping it; he loses his senses of smell and taste, and becomes a woebegone object. In the earlier stages sneezing is often a prominent and very distressing symptom; but as the obstruction increases the mucous membrane becomes less sensitive to tactile stimulation, and the sneezing may disappear altogether.

With his nose troubles the patient may show symptoms of an extensive catarrh of the larynx, trachea, and bronchial tubes; and not infrequently the asthmatic and bronchitic troubles mask the nasal altogether. By some authorities, especially in the German and American schools (Hack, Bosworth, and others), such symptoms are supposed to result from reflex action originating in the nasal mucous membrane; but, so rare is it to find the asthma cured by removing polypi, it is probably more correct to consider the bronchitic and nasal conditions as several local manifestations of a chronic inflammatory process pervading the whole tract of respiratory mucous membrane. And I am prepared to emphasise this view, knowing full well that the rectification of nasal abnormalities other than polypus often results in a most remarkable cure of the bronchial symptoms.

Treatment.—Various remedies have from time to time been suggested for the absorption of mucous polypus, but as a matter of fact they nearly all result in failure. Astringents sometimes appear to have a temporary effect in contracting the size of the smaller growths; and where these consist chiefly in masses of fungating granulation tissue, doubtless the stronger astringents and caustics may be of material benefit. I have found, for instance, zinc chloride (gr. xx. or xxx. ad ℥j.) of considerable service, and chromic acid (gr. x. ad ℥j.) or silver nitrate (gr. xxx. ad. ℥j.) may be equally efficacious; but every such case is infinitely better treated upon ordinary surgical principles. Masses of granulation are best eradicated with the curette, while the larger growths, which we distinguish as polypi, are best removed by the cold snare. Many advocate the use of the incandescent snare, but I fail to see the advantage of it; while risks of scalding from the generation of steam are obvious.

Benign growths of the nose other than mucous polypi.—Besides mucous polypi there are other growths which must at least be enumerated in this place. Those curious cauliflower developments so common in hypertrophic rhinitis, especially as it affects the erectile tissue and the inferior turbinals, actually belong to the section of rhinitis. They consist of erectile tissue infiltrated with large masses of granulation tissue, maintained by some authors to be lymphoid. In old-standing cases they grow more fibrous, and under certain conditions lose their ruddy hue, becoming œdematous and colourless; in this case the fibro-cellular elements become infiltrated with mucin and water, and the growths very closely resemble many instances of ordinary polypus. When finely lobulated and very substantial they have frequently been mistaken for papilloma, and recorded as such.

Papilloma is actually very rare in the Schneiderian membrane; though occasionally small specimens are found, attached to the septum or in the vestibule, which have all the appearance of such growths as found on other distributions of mucous membrane. I have seen a few examples of well-developed papilloma covering the surface of a long-standing mucous polypus, when projecting between the alæ and constantly exposed to the friction of the handkerchief. Such a development has no connection whatever with any tendency in the parent growth to originate malignant disease.

Malignant disease of the nasal cavities.—Malignant disease of the nose falls rather within the domain of the surgeon, and needs but little notice in these pages. According to Erichsen, the transmutation of mucous polypus into epithelioma is by no means a rare occurrence. That this is an error is an opinion which I believe every author will now accept. After having treated more than a thousand cases of polypus, I have never seen these benign growths degenerate into malignant, although I have seen sarcoma and mucous polypus associated in the same nasal fossa. Sarcoma is decidedly commoner in the nose than epithelioma; and I may add, as a characteristic of the former in this region, that its malignancy is probably more difficult to estimate on microscopical examination than in other regions. Cases have been recorded of complete cure of sarcoma by intra-nasal operation alone. I am watching a patient of my own who presented every symptom of malignancy, both clinical and microscopical, in whose case the surgeons declined to interfere, yet for over four years now he has presented no indications of recurrence. The treatment was entirely intra-nasal, and extended over three years; the tendency to recurrence, at first extraordinarily rapid, gradually diminished until it has ceased now, I believe, altogether. Probably all the cases of so-called fibrous tumour found in adolescents, which make such frightful local ravages, separating and protruding the eyes, flattening the nose, and producing "frog-face," are actually sarcoma. Enchondroma has also been described as a cause of like symptoms.

Affections of the nasal bones.—The pathological conditions encountered in certain conditions of inflammation, as it involves the osseous structures of the nose, are inseparably associated with the subject of polypus. That simple inflammation, unsupported by any constitutional dyscrasia, may result in exposure of bone is a fact which can no longer be disputed. As I have said, wherever we find granulations or polypi filling the middle meatus, and attended by suppuration, careful insertion of a blunt probe into the diseased region will readily reveal patches of carious bone. But the cases are extremely rare in which the inflammation is sufficiently intense to set up more than a superficial molecular necrosis. Undoubtedly at times a sequestrum may be produced, although, so far as I am aware, never of any more important part than a fragment of the free border of one or other turbinated bone. Whenever large sequestra are discovered there can be little doubt as to the syphilitic origin of the disease. So far we are unacquainted with any essential differences from similar processes in other bones: the same inflammatory mischief which, in one spot, led to the substitution of a layer of granulation tissue for the normal periosteum, may in adjacent spots produce an accumulation of osteoclasts, causing extensive absorption of bone; or yet again may lead to a more chronic process which has been called by Billroth *osteophytic periostitis.* So far as I am aware, the majority of cases of caries in the nose have not been attributable to tubercle.

But there is yet another condition of bone disease observed, so far as I know, only in the nose, the pathology of which has not yet been satisfactorily studied. We may occasionally detect by the probe an extensive surface of bare bone, uncovered even by granulations, not presenting the roughness of an ordinary sequestrum, and, so far from being friable, of an ivory hardness. Suppuration occurs from the neighbourhood of these exposed surfaces, if not actually from them, and there are always granulations in the vicinity. Such conditions I have watched for many months at a time without the formation of a sequestrum. Probably the phenomenon is due to a gradual interstitial condensation of bone with encroachment upon the Haversian canals, and even obliteration of them; thus depriving any rudimentary granulation of its necessary blood-supply, and reducing suppuration to a minimum. But the process of condensation is so gradual that no attempt at repair is made by throwing off the necrosing surface; and possibly the very condensation minimises the risks of local infective processes, and lessens the danger of extension. In some such manner we may perhaps account for the rarity with which these diseases extend into the cranial cavity. *Osteophytic periostitis* may lead to the most extraordinary overgrowths of the bone itself, more especially when it affects the middle turbinal. The hypertrophy of the free border of this bone is indeed sometimes so exaggerated as to bring it in contact with some portion of the under surface, where such extensive adhesion may take place as to enclose a perfectly sealed space lined, of course, with mucous membrane continually pouring out its secretion. This is one of the methods in which the rare and curious *osseous cyst* is formed, which sometimes assumes such a magnitude as to fill the fossa completely, and even to widen the bridge of the nose, separate the orbits, and induce so much deviation of the septum as to block the other nasal fossa also. Such cysts necessarily have walls the thickness of which is in inverse ratio to the volume; while the contents vary from a thin mucus to a dense atheromatous matter. Occasionally small polypi are found studding both inner and outer surfaces.—G. MacD.

Rhinoscleroma.—This disease, which is exceedingly rare, was first described by Hebra in 1870.

Etiology.—Very little is known of the conditions under which rhinoscleroma originates. The majority of cases have occurred in the south-east of Europe. A few cases have been reported in Central America, Egypt, and India. The first case shown in this country was that of a Guatemalan, aged 18, who was brought before the Pathological Society by Dr. Payne and Sir F. Semon in 1884. The somewhat narrow geographical distribution of the disease would seem to point to some endemic condition as its cause. An instance of the transference of the disease by contagion has been reported.

Morbid anatomy and pathology.—The sites of predilection of the scleroma are the cartilaginous part of the nose, the commencement of the bony part of the nasal cavity, the choanæ and the larynx below the glottis. Each of these places may be affected independently, and not by extension from one part to the other. In exceptional cases the neoplasm has started in the pharynx or hard palate. The disease may be considered as a chronic infective granuloma; that is to say, a round-celled infiltration and a large amount of fibrous tissue are present; there are also numerous larger cells and spaces, "vacuoles," formed by hyaline degeneration of the larger cells. Micro-organisms, first observed by Frisch, resembling in many respects Friedländer's pneumococcus, are found in larger cells, the vacuoles, blood-vessels and lymphatics of the affected part. They can be stained by Gram's method. Inoculation experiments on animals have given no very definite results.

Symptoms.—Necessarily the symptoms vary according to the part affected. Out of eighty-five cases the mucous membrane of the nose was attacked in eighty-one, the cutaneous covering of the nose in seventy-four, the pharynx in fifty-seven, the larynx in nineteen, the trachea in five, the upper lip in forty-six, the upper jaw in sixteen, the hard palate in seventeen, the tongue in four, the lower lip in two, the lachrymal tract in five, and the ear in one case. When the nose is affected, obstruction, which may be complete, is the symptom chiefly complained of; there may be some discharge and even a little bleeding. Pain is usually absent, but there may be some tenderness. The neoplasm occurs in slightly elevated plates or nodules of a red colour, smooth on the surface, and as hard as cartilage. In very exceptional cases the growth has been somewhat soft and of a polypoidal appearance. In the larynx scleroma may cause urgent dyspnœa, and Bandler has shown that chorditis vocalis inferior hypertrophica is simply a variety of the same disease. Evidence is strongly in favour of the view that Stoerk's blenorrhœa is scleroma of the upper air-passages.

Diagnosis.—Rhinoscleroma may be distinguished from lupus, tuberculosis, malignant disease, and syphilis by its slow progress and by the absence of ulceration and offensive discharge. The want of response to an antisyphilitic treatment will confirm the diagnosis as against syphilis. There may be some difficulty in distinguishing keloid from rhinoscleroma; but the former is rarely met with in the nose. The crucial point, however, in the diagnosis of rhinoscleroma is the detection of the characteristic bacilli in portions of the growth removed for the purpose.

Prognosis.—The disease is a very chronic one, and cases are on record in which it has existed for upwards of twenty years. The only dangerous variety is that which attacks the larynx. Cases have been reported in which a complete involution of the growth, verified by microscopic examination, has taken place after an attack of fever; in one instance the fever was typhus, in another possibly of malarial origin.

Treatment.—Attempts have been made, but with very partial success, to maintain the patency of the nose by means of the galvano-cautery and knife. Good results have been reported from injections of 1 to 12 per cent solutions of arsenic into the affected part; a 2 per cent solution of carbolic acid has been used in the same way. The two latter methods are worthy of trial. If stenosis of the larynx be threatened, tracheotomy must be performed.

Glanders.—The nose may be affected in the acute form, to which the name glanders was at one time restricted; or it may be attacked during the course of the chronic form (the farcy of horses).

The disease is frequently contracted by the secretion of the nasal mucous membrane of the diseased animal coming in contact with the nasal mucous membrane of the patient. In these cases the earliest symptoms are met with in the nose. At first a thin mucus is secreted, and the nose becomes swollen, red, and painful; the swelling may extend to the face. After a time the discharge becomes thicker, muco-purulent, stained with blood and very offensive, and the nostrils may be blocked with crusts. The nasal mucous membrane is greatly swollen, and the lining membrane of the accessory sinuses is similarly affected. In some of the chronic cases tubercle-like nodules form and lead to ulceration of the mucous membrane and necrosis of the septum. The nose is not so generally affected in man as in the horse; the disease may run its course without implication of the nose, or the nasal mucous membrane may not be involved until the later stages of the disease in the second or third week.

Diagnosis.—If the nose be early affected and the disease run a rapid course the diagnosis is easy, especially if the patient's occupation be connected with horses. In the more chronic forms the nasal affection may be confounded with tuberculosis or syphilis; but the cutaneous affections of glanders are not seen in tuberculosis, and the disease does not yield to anti-syphilitic treatment. Moreover, the characteristic bacilli of glanders should be sought for in the morbid secretions. For further information the reader is referred to the article "Glanders" in this work (vol. ii. p. 513).

Treatment.—All that can be done locally is to keep the nostrils clean by frequently spraying them with such antiseptic solutions as weak solutions of creasote, carbolic acid, or permanganate of potassium. The occasional application of solution of nitrate of silver or tincture of iodine may be tried.—F. de H. H.

NASAL NEUROSES.—**Olfactory Neuroses.**—The olfactory nerve is the nerve of the special sense of smell. Numerous nervous filaments derived from the olfactory bulb pass through the foramina in the cribriform plate to the mucous membrane of the upper part of the septum and of the outer walls as far down as the middle turbinated body, and to the olfactory cells of Max Schultze from which the fine terminal filaments pass through the external limiting membrane of v. Brunn, to lie between the columnar epithelial cells. The mucous membrane here is peculiarly soft, thick, delicate, pulpy and highly vascular. For the normal perception of odours it is essential that the odoriferous particles should reach the mucous membrane of the upper part of the nasal passages, and that these should be in a moist condition; thus any local abnormality preventing inspiration through the nasal passages, or the presence of polypi or collections of mucus and secretions, or a permanently dry condition of the mucous membrane, will interfere with the sense of smell or completely destroy it.

The terminal filaments of the olfactory nerve may be impaired in various chronic conditions of the mucous membrane, inflammatory and degenerative; thus in chronic rhinitis, or as the result of irritating injections or sprays, or douches, there may be more or less defect of smell.

In testing the sense of smell it is imperative to exclude substances, such as ammonia, which act on the nerve of common sensation; lest we confuse olfactory and purely sensory impressions. Musk or some such scent should be used as the test.

Anosmia, or complete loss of the sense of smell, is frequently observed in polypus cases, as a consequence of disease of the fifth nerve; or in the dry atrophic condition of the mucosa in atrophic rhinitis. It may be either unilateral or bilateral; and may result from congenital defects, blows or falls on the head producing fracture of the cribriform plate, basilar meningitis, intracranial tumours, syphilitic disease, embolism or hæmorrhage of the middle cerebral artery, or from the less gross central lesions associated with epilepsy, locomotor ataxia, general paralysis, hysteria and insanity. A few cases of unilateral destruction of the olfactory bulb with anosmia are recorded, and in these the left bulb has always been the one affected. Anosmia is very rarely detected in intracranial hæmorrhages or tumours, as in the few cases in which the sense of olfaction is interfered with their effect is almost always unilateral. Anosmia has been observed to follow the removal of both ovaries.

Parosmia, or perversion of the sense of smell, in which imaginary or subjective perceptions of odours are present, is usually central. It occurs in hysteria, hypochondriasis, epilepsy, influenza, and lesions of the anterior temporal lobes; it is important to know that it may be the first, or one of the first, signs of mental derangement. Olfactory hallucinations have been known to occur in cases of sexual neurasthenia.

Hyperosmia, or hyperæsthesia of the olfactory nerve, with increased sensitiveness to smell, may arise in neurasthenic conditions with exaggeration of all nervous impressions, in hysteria and hypochondriasis, or as the result of irritative lesions affecting the olfactory bulbs.

The prognosis in anosmia will depend very much on the special cause of the loss of the sense of smell. If it be due to nasal polypi, or other removable causes, the prognosis is favourable, provided the loss of function have not persisted for a long time; after two years the sense is seldom regained. But when associated with degeneration of the mucous membrane, as in syphilitic disease or atrophic rhinitis, the olfactory end organs soon become atrophied and the prognosis hopeless. Loss of smell due to organic central nerve lesions will rarely be restored; on the other hand, the prognosis in functional anosmia and parosmia, except in cases when this symptom precedes insanity, is generally favourable.

Treatment.—If the neurosis of olfaction be due to local disease this should be treated, and, with the removal of the cause, the functions of the olfactory nerve may possibly be restored; but very little more can be done. Local galvanisation and faradisation may prove useful, and strychnine and arsenic may be given internally.

The treatment of anosmia and parosmia due to central nervous affections resolves itself into the treatment of the various causes of the disease The purely functional cases should be treated by nervine tonics, change of air and rest; while in women any irregularity in menstruation, or otherwise, should receive attention.

Sensory and Reflex Neuroses of the Nose.—A great deal has been recently said and written in reference to the sensory neuroses of the nose That these neuroses occur, and that their effect may be far-reaching, there is now no room for doubt. But while, on the one hand, there has been a tendency on the part of some clinicians to ignore the obvious existence of these diseases, there has been an unfortunate proclivity of late to refer all and sundry obscure neuroses to the nose, and to explain their occurrence as nasal reflex phenomena. We would emphasise the importance of being on our guard against this prevalent error, while giving due regard to the large class of cases that may legitimately be included under the term *nasal neuroses.*

When we remember the intimate anatomical correlation between the nerves supplying the nose and other regions around or more distantly situated, it is easy to conceive that centripetal impulses from the nerves in the nasal passages may have far-reaching reflex effects. The nasal mucous membrane is supplied with ordinary sensation by the ethmoidal branch of the nasal nerve and branches from Meckel's ganglion. This is connected with the Gasserian ganglion, which, in turn, is in relation with the carotid plexus of the sympathetic and perhaps with the pneumogastric. The arterial supply to the mucous membrane and to the erectile tissue of the turbinated bodies is controlled by vaso-motor nerves from Meckel's ganglion, and is under the control of the vaso-motor centres in the medulla.

The physiological nasal reflexes are sneezing, coughing, lachrymation, and vaso-motor changes producing increased secretion. Their intimate relationship with other reflex areas is seen in the effect of bright sunlight on the eye producing lachrymation, coughing, and rhinorrhœa; in the fact that particles of food in the larynx give rise to lachrymation as well as to cough, and again in the reflex cough due to irritation in the ear. In some susceptible persons, if certain portions of the nasal mucous membrane are irritated by a probe, sneezing and lachrymation ensue; and if the turbinals are irritated posteriorly, especially if the Eustachian orifices are touched, cough is often excited. Dust and particles of foreign matter and irritating vapours produce similar effects. The specially sensitive spots—called hyperæsthetic areas—are situated on the posterior extremity of the inferior turbinal and the corresponding portion of the septum, at the anterior extremity of the superior turbinated body, at the anterior extremity of the middle turbinated and the corresponding portion of the septum; to these must be added the lips of the Eustachian tubes. Further, it has been shown that irritation of the nose may produce arrest of respiration and syncope from temporary arrest of the heart's action; similar effects are sometimes observed as the result of strong odours. Unilateral exophthalmos and increased pulse frequency have been observed (Semon) to follow an operation for nasal polypi; it is questionable, however, whether these events stood in the relation of cause and effect.

Hyperæsthesia is generally associated with a more or less definitely abnormal condition of the nasal mucous membrane; often, however, no abnormality can be detected. It is usually associated with sneezing and rhinorrhœa, and is generally the immediate local factor in "hay fever," nasal cough, and so forth. It may be due to any irritation or catarrhal inflammation in neurotic subjects; or it may result from central or from reflex causes in the eye, the ear, or the digestive or genital organs.

Incomplete anæsthesia results from various chronic degenerative diseases of the mucous membrane, and in many cases of polypus. Total anæsthesia may be due to degeneration or destruction of the sensory nerves, as in cerebral tumour or in intracranial syphilis; or it may be functional, as in hysteria.

Nasal cough.—Occasionally cases arise in which there is a hard, persistent, dry cough, which ceases during sleep, due to an exaggeration of the normal nasal reflex cough. It may sometimes be excited by touching the sensitive parts of the nasal mucous membrane with a probe. If there be no pulmonary disease, and no other cause for such a cough can be detected, the possibility of its nasal origin should be borne in mind. Post-nasal growths will also excite it sometimes; but in cases of this class it may be due to irritation in the ear.

Vaso-motor Neuroses.—Vascular engorgement of the nasal mucosa and distension of the erectile tissues, especially of the turbinated bodies, occur in two forms: (*a*) Periodic vascular swelling; (*b*) Vascular engorgement with coryza (vaso-motor coryza), and various reflex neuroses, as in paroxysmal sneezing.

Periodic vascular engorgement and swelling of the erectile tissues is generally associated with nervous prostration or imperfect digestion. The fulness of the nasal mucosa produces more or less obstruction in one or both nasal passages; it comes and goes, and is usually worse at night on going to bed. Very often an examination is made just at the time when the swelling has subsided and nothing abnormal can be detected. If the patient be seen while the nose is obstructed by the turgidity of the tissues the real nature of the affection is readily distinguished from hypertrophic rhinitis on applying a cocaine spray; when vaso-motor swelling entirely disappears. In some cases, particularly in gouty and dyspeptic patients, the engorgement of the mucous membrane is accompanied by redness and swelling of the nose externally and flushing of the face.

These changes are prone to occur—(i.) in persons of the neurotic temperament who have run down from hard brain work; (ii.) in gouty patients; (iii.) from abuse of alcohol; (iv.) in neurotic women, especially at the menstrual period.

The treatment must be mainly directed towards improvement of the general health by nerve tonics, massage, cold baths, and out-of-door exercises. It is sometimes necessary to use the galvano-cautery, linear cauterisations being made over the turbinated bodies; and if chronic rhinitis exist, suitable local treatment will be required.

Paroxysmal sneezing may be due (*a*) to reflex peripheral irritation; (*b*) to a central neurosis. The physiological mechanism of sneezing may be briefly described as a reflex act brought about by irritation of the trigeminal nerve, either in the nasal passages or in other regions which it supplies.

We have met with cases in neurotic women in which it occurred in paroxysms of thirty or forty sneezes, especially on rising in the morning, and when the face was plunged into cold water; and similar cases have been frequently recorded. In a few cases there is no rhinorrhœa; but as a rule there is lachrymation and stuffiness of the nose followed by watery discharge, and a pain in the bridge of the nose. Prolonged attacks are very exhausting.

Paroxysmal sneezing is generally due to a hyperæsthetic condition of the nasal mucous membrane, and it is set up by the irritation of particles of dust.

"Hay fever" is a form of paroxysmal sneezing usually brought about by the irritation of certain kinds of pollen. Some patients are peculiarly susceptible to the effluvia of certain animals—for instance, the cat, horse, or dog, and invariably suffer from sneezing or asthma when in proximity to these animals; others are similarly affected by peaches, violets, musk, peppermint, ipecacuanha, lycopodium, and so on. The exciting causes of paroxysmal sneezing are such that although every one is continually exposed to their influence, yet comparatively few persons suffer; thus it is obvious that individual predisposition is necessary for the occurrence of the affection. Patients are almost invariably of the neurotic temperament, especially dwellers in cities; and there can be no doubt that, to some extent, the predisposition is hereditary. The causes being so general and yet paroxysmal sneezing being relatively so rare, a third factor must be necessary for its occurrence; and in most cases some local abnormalities will be found in the nasal passages, the most frequent being (*a*) hypertrophic rhinitis; (*b*) spurs and bony projections of the turbinated bones or of the septum; (*c*) deviations of the septum; (*d*) polypi; (*e*) old post-nasal vegetations; (*f*) areas of hyperæsthesia in the nasal mucous membrane.

Thus it appears that paroxysmal sneezing is the conjoint result of three factors:—(i.) The predisposing neurasthenic constitutional state; (ii.) an external irritant; (iii.) a pathological state of the nasal passages.

Asthma.—By the law of irradiation of reflex action—by the extension, that is, of reflex action from nerves in which it first appears to neighbouring ones, by means of the communications between the different systems or groups of ganglionic cells—persistent irritation in the nose may result in spasmodic asthma. It has long been known that asthma is sometimes associated with intra-nasal disease, but it is only since Voltolini's classical case of asthma, which he cured by the removal of nasal polypi, that attention has been directed to the causal connection between nasal disease and asthma. Whilst this connection, in our experience, is undeniable, we must again state that at present there is perhaps too strong a tendency to attribute asthma to any slight departure from the normal anatomical configuration of the intra-nasal structures.

No doubt, in a good many cases, it is extremely difficult to determine how far the asthma and the associated nasal phenomena are but different concomitant expressions of a common central neurosis; namely, a peculiar condition of the nerve-centres in which paroxysms may be excited by various peripheral irritations; for paroxysmal sneezing and coryza often precede, accompany, or alternate with attacks of spasmodic asthma. And just as we observe that attacks of asthma by frequent recurrence may eventually lead to chronic bronchitis and emphysema, so we likewise find that paroxysmal sneezing and coryza may result in a form of chronic rhinitis, which is then the consequence but not the cause of the asthma.

Further, we have to consider that when nasal coryza results from the action of some irritant conveyed by the inspired air, it is probable that the lower air-passages, though in a less degree, are simultaneously exposed to its influence; thus the asthma may be due to the latter influence. When the nose is partially or completely obstructed, and respiration oral, the defective filtration and warming of the inspired air will injure the lower respiratory tract. In these cases restoration of the nasal functions by appropriate local treatment will save the bronchial mucous membrane from much of the irritation to which it was previously subjected.

Treatment.—In paroxysmal sneezing and asthma, as in all sensory and reflex neuroses of the nose, treatment should be mainly directed to overcoming the underlying neurasthenia by appropriate nervine tonics—such as phosphorus, iron, arsenic, valerianate of zinc—and by general hygienic measures. The nasal conditions should, of course, be carefully investigated; and if positively morbid changes be detected, such as are reasonably likely to cause the reflex neurosis, these must receive appropriate treatment; but the discovery of a small spur on the septum or of a small amount of erectile swelling on the middle or lower turbinated bones should not be proclaimed at once as the undoubted cause of the malady. Caution is the more necessary in these cases as it is very difficult, and often impossible, to distinguish between the cases in which intra-nasal treatment is likely to prove beneficial and those in which but a temporary effect will be obtained, or none. On the other hand, we may say that a good many cases of paroxysmal sneezing will probably be improved by local treatment; and, in a considerably smaller proportion, that asthmatic paroxysms may be cut short or considerably relieved by spraying a solution of cocaine into the nasal passages. If chronic hypertrophic rhinitis, or polypi, or any other manifest nasal disease be found, it should certainly be treated in the hope that the neuroses may be relieved thereby; but assurance of cure by nasal treatment cannot be given to patients even if the concomitant nasal affection be well marked, for we cannot remove a hereditary or an acquired instability of the nerve-centres. Nevertheless, by nasal treatment we sometimes obtain most brilliant results and perfect relief from all symptoms, particularly in cases in which nasal polypi and bronchial asthma coexist.

In paroxysmal sneezing, when the only abnormality is erectile swelling and vascular injection of the mucous membrane, we may cauterise the swollen parts superficially. The best plan is to ascertain, before applying cocaine, if there are any sensitive spots, and then to cauterise these after the cocaine has been applied.

A method followed by one of us (W. W.), with most gratifying results, is to spray the nasal passages cautiously with an aqueous solution of "iodic hydrarg" (a combination of the iodides of mercury and potassium) of the strength of 1 part in 100. A cocaine spray should be used beforehand, but, as the cocaine is destroyed by the mercurial salt, it is necessary to relieve the pain which very rapidly ensues by a hypodermic injection of morphine. The solution is intensely irritating, and care is necessary lest it get into the eyes or into the throat. The mucous membrane of the nose becomes much congested and swollen. In about three hours the pain and swelling subside, and are followed by a simple nasal catarrh lasting two or three days. In suitable cases, if this be efficiently done at the onset of the symptoms of that form of paroxysmal sneezing distinguished by the name of "hay fever," the patient will remain free from symptoms throughout the season; and there are very few persons who have suffered from the affection who will not readily undergo this or any treatment that offers a fair prospect of relief. This method has the advantage of leaving the sense of smell unimpaired, and involves no destruction of tissue. It may have to be repeated the following year, but in some cases the relief has extended over several years.

Cocaine should never be recommended as a routine method for the relief of paroxysmal sneezing. It tends to aggravate the condition after its transient effects have passed off. Moreover, serious symptoms of acute cocaine poisoning may suddenly declare themselves, even after the patient has to all appearances become quite accustomed to the use of the drug. [*Vide* art. "Cocaine," vol. ii. p. 904.]

Idiopathic rhinorrhœa is a name applied to an affection in which the prominent symptom consists in a profuse watery discharge from the nasal mucous membrane. While the group of cases comprised under this heading are probably due to a variety of etiological factors, they are all essentially vaso-motor neuroses. In some cases the copious discharge is the only symptom; in others it is accompanied by sneezing and lachrymation, and is in fact a form of paroxysmal coryza and sneezing in which the coryza is the prominent feature. In most cases the patients are of neurotic temperament; physical shock, hard brain work, exposure to cold, are the chief exciting causes to which it has been attributed; but in other cases it comes on suddenly without apparent cause. In a case recorded by Dr. Althaus it was associated with anæsthesia of the regions supplied by the fifth cranial nerve. In a case recently reported it was associated with disease of the pituitary body; usually, however, its cause has remained in obscurity. Sometimes this rhinorrhœa is an escape of cerebrospinal fluid through the nose. In such cases, which appear to be more frequent than hitherto supposed, the discharge is usually unilateral, and its quantity sometimes very considerable.

The symptoms may begin with some itching or pricking sensations in the nose. When the discharge has continued for some hours the mucous membrane becomes swollen and œdematous. The copious clear colourless or slightly yellow discharge consists of water with traces of chloride of sodium and mucus. The amount varies very much; in some cases as much as two or three quarts have come away in the twenty-four hours.

In the intervals between the periodic attacks the mucous membrane resumes its normal aspect; but when the affection has existed for a considerable time the mucosa becomes sodden and there is a tendency to mucous polypi. The disease may recur for months or years, but eventually it nearly always ceases spontaneously.

Coryza œdematosa is very closely allied to idiopathic rhinorrhœa. It consists of a serous infiltration into the connective tissue of the inferior and middle turbinated bodies, which is sometimes migratory and suddenly appears in other regions supplied by the trigeminus as it leaves the nasal passages. It is apparently connected with some irregularity of digestion in neurotic subjects.

No treatment appears to have any lasting results. Galvano-cauterisation of the turbinated bodies may give relief, but local treatment is generally without any lasting effect. General hygienic measures and constitutional treatment should be adopted.

Epilepsy is said to have been due in some instances to intra-nasal disease, the treatment of which relieved the patient of this grave neurosis.

Many other neuroses—such as tinnitus, vertigo, headache, chorea, asthenopia, Graves' disease, facial erythema—have been attributed in like manner to intra-nasal disease. The possibility of their occurrence must be admitted, but such cases are at most extremely rare.—F. S. and W. W.

Foreign bodies in the nose.—Foreign bodies may find their way into the nasal passages under various circumstances. Children frequently put foreign bodies up their noses; hysterical women and lunatics may do the same. Bullets and portions of knives and other sharp instruments, penetrating the skin, have thus entered the nasal fossæ. Plugs introduced to control epistaxis have occasionally been forgotten. In some cases a foreign body has been forced into the naso-pharyngeal cavity in the act of vomiting. Among the most common articles met with in the nose are fruit stones, beans, buttons, beads, pieces of wood or slate pencil, shells or pebbles. A supernumerary tooth sometimes erupts into the nasal cavity.

Symptoms.—The symptoms depend in great measure upon the nature, size, and shape of the foreign body. As a rule, the presence of a foreign body in the nose sets up a discharge which at first is muco-purulent; but it may become fœtid and tinged with blood. In most cases pain is complained of, and the pain may radiate over the side of the face. Where the foreign body is large, or has caused much swelling, there is obstruction of the affected nostril. There is often sympathetic disturbance of the eye and ear, as shown by increased secretion of tears, earache, tinnitus, and even otitis media. The voice may have a nasal twang, and attacks of sneezing, giddiness, and vomiting have been described. Delirium has occurred in a child. In process of time toleration may be established, and instances have been recorded of foreign bodies lying in the nose for many years without giving rise to any marked symptoms.

Diagnosis.—The existence of a unilateral purulent, fœtid, or bloody discharge from the nose, especially in a child, should always lead us to suspect a foreign body. If there be any doubt in the matter, careful spraying of the nose, and the use of the probe after cocainisation of the nasal mucous membrane, will usually clear up the diagnosis. If the patient be a child it may be necessary to give a general anæsthetic in order to make a satisfactory examination without injury to the soft parts.

Treatment.—In most cases the foreign body can be removed most readily by means of the forceps or the snare. A modification of Leroy d'Etiolle's instrument used in aural cases, or a strabismus hook, may be employed for the same purpose. Gross' nasal spud or probe, with corkscrew point, will be found useful for the removal of peas and other soft substances. Should it not be possible to remove the foreign body anteriorly, it may be necessary to push it backwards into the pharynx; while doing so the operator should introduce his finger into the patient's throat, so as to prevent the body passing into the larynx.

For all these procedures the nasal mucous membrane should be anæsthetised with a 20 per cent solution of cocaine. If the patient be a child, his arms should be secured by a shawl wrapped round them, or a general anæsthetic should be given. The pneumatic method sometimes answers; this is best effected by introducing the nozzle of a Politzer's bag into the patient's nostril, and then suddenly compressing the bag as the patient swallows some water, as in inflation of the Eustachian tube.

The attempt to expel the foreign body by a stream of water passed into the unobstructed nostril is attended with serious risk of setting up otitis media by the entrance of water into the Eustachian tube. The administration of sternutatories is another plan which had better be avoided.

Rhinoliths.—This name has been applied to the deposition of calcareous matter within the nose, forming a stone or nasal calculus.

Etiology.—Women are much more subject to this affection than men. Of 110 cases collected by Seeligmann, 62 occurred in women, 29 in men; in 9 the sex was not recorded. No obvious explanation of this preference is forthcoming; it has been suggested that women blow their noses less than men, and that consequently there is a greater liability in them to retention of secretion.

Rhinoliths gradually increase in frequency above the age of ten; but they are occasionally met with under this age. Concretions of a characteristic form are frequently found in the nostrils of cement-workers; chiefly in those who are engaged in raking out cement-ovens, and who consequently inhale hot cement dust.

In the great majority of cases the concretion takes place round some foreign body, which may have been introduced into the nostrils, or may have entered through the choanæ in the act of vomiting or sneezing. The nucleus may consist of a bead, button, or other foreign body. In some cases it is represented by a piece of inspissated mucus, or a blood-clot.

Three conditions seem to promote the formation of these concretions —(i.) An abnormal condition of the nasal and lachrymal secretion; (ii.) Any condition, such as nasal stenosis, which leads to retention of the secretion; (iii.) The presence of micro-organisms: this last condition may depend upon the two former. Micro-organisms attract the lime salts of the nasal mucus and favour their deposition on the foreign body. Usually one stone only is found; and the exceptions to this rule are more apparent than real, the second stone being probably a small mass detached from the first in the process of extraction. Cases, however, have been recorded in which two stones were found; and in one or more cases a stone has been found in each nostril. The average weight of rhinoliths is from 7 to 90 grains: a case of a stone weighing 720 grains has been recorded. In colour, rhinoliths vary from a dirty white to gray, brown, or black. They may be soft and crumbling, or as hard as ivory. Chemically, rhinoliths are composed chiefly of the phosphates and carbonates of calcium and magnesium, with traces of the chloride and carbonate of sodium, and a certain proportion of organic matter. Traces of iron have been detected occasionally, probably in cases in which the nucleus was composed of that metal.

Symptoms.—The symptoms due to the presence of a rhinolith are similar to those caused by a foreign body in the nostril. Inasmuch, however, as the rhinolith grows slowly the symptoms come on slowly. The most usual symptom is a unilateral discharge, generally muco-purulent, but occasionally fœtid. In exceptional cases, where the septum has become perforated, there may be discharge from both nostrils.

Diagnosis.—For the detection of a rhinolith the nose must be examined as directed under the heading "Foreign Bodies in the Nose." In some cases the rhinolith becomes so embedded in the mucous membrane that it may be mistaken for a polypus, or even a cancer. The purulent discharge may excite fear of necrosis, or it may be put down to ozæna.

Prognosis.—The removal of the rhinolith is almost invariably followed by an immediate cessation of the symptoms it had produced.

Treatment.—The removal of a rhinolith is effected in the same manner as that of any other foreign body in the nose.

In cases in which the rhinolith is hard, and very large, it may be impossible to remove it without separating the nose from its attachment to the cheek; attempts to lessen its bulk may be made by the application of hydrochloric acid.

Maggots in the nose.—This disease is almost entirely confined to the tropics; a very small number of cases have occurred in Europe.

In India, where the disease is called "Peenash," it is fairly common; but this name is used rather loosely to include several affections of the nose not necessarily indicative of the presence of maggots.

The fly is the Lucilia hominivora, or the Sarcophaga Georgina; to the larva of the latter the term "screw-worm" has been applied. In rare instances the larvæ of other flies have been met with in the nose.

The fly commonly enters the nostril during sleep. As a rule, patients suffering from ozæna are attacked. The flies are probably attracted by the smell, and they find a ready entrance into the capacious nostril of patients with atrophic rhinitis. It would appear that the larvæ are deposited in healthy nostrils accidentally.

The larvæ develop very quickly and in enormous numbers. In one case 388 maggots were counted. The symptoms which first appear are excessive irritability of the pituitary membrane, sneezing, and a sanious discharge from the nostrils. In some cases epistaxis occurs. In severe cases intense frontal headache, anorexia, and fever with delirium are met with. The nose and face are swollen, and the larvæ may be seen escaping from the nostrils. Not only the mucous membrane of the nose, but even the cartilages and bones of the nose may be destroyed, so that death may occur from the meningitis of septic poisoning, or of direct extension from the sphenoidal and ethmoidal sinuses invaded by the larvæ.

The prognosis is always a grave one; for instance, out of seven cases occurring at Fort Clarke, in Dakota, all were fatal except one. This is, however, an exceptionally high mortality.

Treatment.—The only effectual method of treatment is the use of chloroform. At the very beginning of the disease, and in slight cases, the inhalation of chloroform may suffice. In more severe cases the patient must be anæsthetised, and the nostrils syringed out with a mixture of equal parts of chloroform and water, or with pure chloroform. Spraying the nose with a one in forty solution of carbolic acid in oil will relieve the pain produced by the injection of pure chloroform.

Centipedes, caterpillars, earwigs, leeches, and ascarides have occasionally been known to take up their abode in the nose. The symptoms produced are those common to the presence of any foreign body, with the addition that the movements of the visitor give rise to excessive formication in the part. In the case of the leech epistaxis has been noticed as a symptom.—F. DE H. H.

Diseases of the accessory sinuses of the nose.—Practically speaking, we may disregard in this place all affections of the accessory cavities other than suppuration; it is sufficient to bear in mind that polypus, cystoma, fibroma, osteoma and malignant disease—sarcoma more especially, may originate in any of these regions.

Suppuration in the accessory sinuses of the nose.—The large majority of these cases is intimately associated with, if not actually secondary to one or other of the affections considered in the previous sections; and as, with such an association, two or more of these cavities are often simultaneously involved, it is neither desirable nor expedient to dissociate altogether the etiology and symptoms of the different localities. Yet for clinical reasons the conventional classification must be followed to a certain extent, although we may briefly mention here certain points of causation common to all these sinuses. The only predisposing factors are such as have been enumerated in speaking of polypus and bone disease; and any conditions favouring a development of the catarrhal state may lead, if unchecked, to the implication of one or more accessory cavities in the simple catarrhal process, and, secondarily from retention or increasing intensity of the inflammation, to suppuration, abscess, granulation, and polypus. Probably any local peculiarities interfering with free drainage, such as extreme narrowness of the fossæ, or distortions of the septum, may be quoted as predisposing factors.

Empyema of the Antrum.—A small war has long been raging among rhinologists as to whether disease of the nose or of the teeth is the commoner source of suppuration in the antrum; the dentists, I need hardly add, hold to the latter view. But those specialists who have worked most conspicuously at the subject appear to support the opinion, strongly maintained by myself, that the immense majority of such cases originates in suppurative conditions of the nasal mucosa, or is associated with it. Among our supporters we may count Zuckerkandl, Ziem, Hartmann, Krause, Gouguenheim, Baratoux, and others; while the alternative opinion is supported by the surgeons and dentists, and, among specialists, by Semon, M'Bride, Fraenkel, Moritz Schmidt, Schech, and others. I believe the discrepancy of opinion is easily accounted for when we remember that, only a few years ago, empyema of the maxillary sinus without swelling of the face was overlooked unless there were an obviously carious tooth to account for the fœtid discharge from the nose; whereas in all cases associated with polypus, the latter, together with the general catarrhal state of the mucous membrane, was supposed sufficient to account for the discharge. Moreover, with certain observers, I am convinced it has become a custom to accuse any coexisting carious tooth of being the prime source of the mischief; and most people either have, or have had, carious molars or bicuspids in the upper jaw.

But apart from these two methods of causation, there undoubtedly exists a considerable number of cases where abscess originates in the antrum, primarily as the result of catching cold; such cases are not necessarily attended by the symptoms of pain, swelling of the face and fever, first described, I believe, by John Hunter, and quoted in the text-books of surgery.

Finally, to our humiliation, it must be admitted that occasionally suppuration in the antrum has followed removal of the middle turbinated bone, injudicious cauterisations, and probably other operations.

The usual symptoms for which the patient seeks relief are unilateral and frequently fœtid discharge from the nose, and occasionally more or less severe supraorbital neuralgia. This pain generally assumes a curious periodicity, appearing regularly at the same time each day, and persisting for the same number of hours; it is not obviously associated with increasing accumulation in the cavity, nor does augmented discharge seem to account for its cessation: nevertheless it ceases altogether on the surgical evacuation of the abscess. In exceptional cases the pain is referred to the cheek; and we may sometimes elicit it by percussion over the malar bone, the side of the nose, or the frontal region. Rarely the discharge finds exit only into the post-nasal space, a fact which has occasionally (in two cases in my experience) led to an erroneous diagnosis. A point worthy of note is that, the patient's olfactory sense being intact, he is perpetually haunted by the evil odour himself; although it is often not sufficiently pronounced to be perceptible by his friends. On the other hand, in ozæna, or atrophic rhinitis, the unpleasant smell gives no trouble to the patient himself, whose olfactory sense is seriously impaired, although it often makes him intolerable to his friends. Beyond the local symptoms there is frequently some general disturbance of health, especially if the discharge has continued for many years; the patient grows anæmic; partly, no doubt, from mental distress at the perpetual stench which he cannot forget and cannot be persuaded to believe is imperceptible to others. The discharge is occasionally intermittent and small in quantity; at other times continuous and extraordinary in amount. Generally it flows out more readily on lowering the head, a point of some service in diagnosis. Rarely the disease is bilateral, and then is generally symptomatic of bilateral ethmoidal disease.

In passing to the objective symptoms, it is wise to bear in mind the fact that there may be considerable difficulty in making a positive diagnosis. Some cases are fairly clear, yet in none are the conditions absolutely pathognomonic, for the main point in diagnosis is the situation of the discharge as it is seen lying in the nose. Whenever, in fact, we perceive an opaque canary-coloured purulent discharge (which must be carefully distinguished from the transparent muco-pus of simple rhinitis) lying in the concavity of the middle turbinal, which discharge, after being wiped away, is immediately reproduced, and especially on lowering the head between the knees, we need have but little hesitation in opening the antrum with the tolerable certainty of evacuating pus. Yet it must be remembered that the frontal sinus and the anterior ethmoidal cells also open into this region, and almost at the same point—an inch or so back from the anterior extremity of the middle turbinal—and that consequently suppuration in any of these cavities would yield a similar appearance. As a matter of fact, it is even possible that, in the event of pus originating in the anterior ethmoidal cells or infundibulum, the antrum will prove to be a receptacle of pus, even if not directly involved in the disease.

A means of objective investigation recently added to our list by

Voltolini consists in a method of transillumination first employed by that observer for diagnosing thickening of the alæ of the thyroid cartilage in perichondritis of the larynx. The method now usually employed, which has been elaborated by Heryng, and later by Davidson, is as follows:—A five-volt lamp is attached to the extremity of a tongue depressor, the lingual portion of which is constructed of some non-conducting material such as vulcanite; this is inserted into the mouth and the tongue depressed, while the patient closes the lips firmly round the instrument. The room is now totally darkened and the circuit of the current is completed. Immediately a rosy red light suffuses the face, the cheeks and lips being the most brilliant, though often brightest immediately under the eyes. It is essential to the success of the procedure that the room should be absolutely dark. According to Heryng's observations, whenever there is pus or a solid tumour in the antrum, that side of the face, especially above the malar prominence and beneath the lower eyelid, is less bright than the other; while in cystic disease, on the contrary, the side affected will be the more brilliantly illuminated. This latter point had been discovered by Voltolini, who was thus enabled to diagnose a cyst in a case supposed to be a sarcoma; the patient having been doomed to the removal of the superior maxilla.

I believe the general opinion in regard to transillumination of the antrum now is that it gives no more positive evidence of the presence of pus than do other objective signs. Nevertheless in a disease in which no one point can be relied upon, any additional evidence must be of considerable value. Such being the case, it may be justly admitted that many cases cannot be satisfactorily investigated without this method. Besides, it is so simple, and needs so little special experience, that it may often be of value to surgeons of little skill in the examination of the nasal fossæ. Yet it must be acknowledged that probably its most striking service is in the diagnosis of cystic from solid tumours of the antrum.

In syphilis of the nose a unilateral fœtid discharge is generally due to a sequestrum, which can usually be detected in the neighbourhood of the vomer or turbinated bodies by the help of a probe; there is often perforation of the hard palate also. Rhinolith may give rise to identical symptoms. Simple caries, with the exposure of small portions of bone, leads to no fœtor, provided the exit of the pus be not interfered with. In empyema of the sphenoidal sinus, as well as in disease of the posterior ethmoidal cells, the pus makes its exit into the post-nasal space, and is accidentally, as it were, blown into the nose. In the case of malignant disease of the antrum there may be a purulent discharge from the nose; but the usual signs of distension of the cavity will be present, and this, together with the history of the case, will prevent any error in diagnosis. In case of difficulty it may be remembered that in abscess the swelling, if any be present, subsides as soon as the pus is evacuated. Finally, it must be admitted that a positive diagnosis can be made only by adopting one of the different procedures for opening the cavity.

The treatment of empyema of the maxillary sinus has of late years given rise to as much divergence of opinion as the etiology; though, before the nose was made a region of special study, no one attempted to improve upon Hunter's method of tapping the antrum. This consisted in removing one of the molars, and breaking down, with a gimlet or drill, the thin layer of bone between the alveolus and the cavity above. Hunter, too, refers to the alternative of making an opening from the nose into the antrum, though he does not dwell upon it even for the sake of indicating its disadvantages; these are, chiefly, the difficulty in the subsequent drainage—the opening not being in the most dependent portion of the cavity, and in the irrigation of the cavity.

Suppuration in the frontal sinus and ethmoidal cells.—I have already said that a few years ago I considered empyema of the frontal sinus so rare that we were unable to give any satisfactory rules for its diagnosis; apart, of course, from those cases where complete retention of secretion led to external swelling and pain: but more extended observation has convinced me that many cases which I used to consider as ethmoidal suppuration are actually due to mischief in the frontal sinus I must admit, however, that the association of the two conditions is common enough, while it is by no means rare for the frontal sinus, anterior ethmoidal cells, and antrum to be involved simultaneously.

A brief reference to the anatomy of the parts will make the etiology and diagnosis more intelligible. The frontal sinus is continued downwards and backwards into the passage known as the infundibulum which, having one or more accessory cells communicating with it, passes externally to the anterior extremity of the middle spongy bone's attachment, on its outer side traversing the inner wall of the antrum till it opens in the middle meatus at the semilunar hiatus. I believe that many a case of suppuration in the frontal sinus begins in an inflammatory occlusion, more or less complete, of this opening; whence we have the one essential factor for the production of abscess. The infundibulum is probably often involved before the mischief extends into the middle meatus, to such an extent as to occlude and distend it, giving rise to the appearance of a duplicated middle turbinal. Indeed this appearance has been erroneously described as a cleavage of the middle spongy bone, and as symptomatic of the somewhat hypothetical "necrosing ethmoiditis" (Woakes). Retention of simple mucus in the infundibulum possibly gives rise to some cases of osseous cysts and I have seen three or four instances of abscess confined to the infundibulum: occasionally these abscesses, instead of rupturing externally, make an exit into the antrum and thus convert the case into abscess of the latter sinus. Or the mischief may gradually extend upwards, when the mucous membrane of the infundibulum disappears and is replaced by granulation tissue, which further obstructs free drainage; the accessory cells of this region partake in the process, and in time the cavity of the frontal sinus becomes similarly involved. But during the whole history of such a case, although the flow of the discharge is sufficiently obstructed to cause distension of the thin-walled infundibulum, yet retention may at no time be so complete as to attenuate the denser parietes of the frontal sinus; so that it is only in the rarest cases that slowly progressing disease would give rise to the generally accepted symptoms of acute frontal abscess.

The etiology of disease beginning in the ethmoidal cells is not materially different. A small abscess may arise during an attack of acute rhinitis, which abscess, if the patient be constantly suffering from attacks of the initial mischief, becomes chronic; and thus is initiated the whole train of symptoms which may end in such extensive disease as I have described. Besides simple inflammation, a rhinolith may be the starting-point of abscess in the frontal sinus or in an ethmoidal cell; or phosphorus poisoning, tuberculosis, or syphilis may be concerned in the case. Rarely such suppuration is observed in conjunction with erysipelas (Zuckerkandl, Weichselbaum).

I have latterly become convinced of the fact that the point in diagnosis upon which formerly we chiefly relied for diagnosing suppuration of the antrum, namely, the reproduction of pus in the middle meatus by hanging the head forwards and rotating it, is actually quite as often indicative of suppuration in the frontal sinus. While many rhinologists will admit that the symptom is by no means pathognomonic of antral disease, yet I believe most would doubt its frequent occurrence in the frontal disorder; yet I am prepared to affirm that such is the case. It is not altogether easy to account for the phenomenon, seeing that in the upright position of the head the opening is at the lowest point. When we remember the narrow passage of the infundibulum, more or less obstructed as it generally is in these cases by granulations, we may liken the condition to that of a beer-barrel with the tap turned on but the vent-peg tight in the bung; unless we remove this peg the only way to ensure entrance of air will be to invert the whole barrel from time to time. In the case of the frontal sinus, I have again and again elicited this symptom after washing the antrum free of all suspicion of pus; and the large quantity poured out of the frontal sinus on such occasions, by tilting the head forwards or between the patient's knees, has been sufficient to preclude a possibility of its flowing from any of the smaller ethmoidal cells.

As a matter of fact, in most of these cases, when more than one cavity is simultaneously and similarly affected, I doubt if it be ever possible, except in the case to be immediately considered, to be convinced of the fact of frontal suppuration before we have shown by surgical measures that the antrum is sound; and it may even be necessary to eliminate ethmoidal suppuration also before we are certain as to the frontal.

The one sign which may make a diagnosis quite clear in frontal abscess is that when the inner walls of the infundibulum have undergone absorption, the point at which the pus makes its exit is brought so much forwards that a probe with a slight anterior curve may be passed up into the cavity; or a long, fine Eustachian catheter may be passed up and the abscess irrigated: the diagnosis will then be positive. In other more doubtful cases some help may be gained by transillumination. A small five-volt lamp with condenser is enclosed in a cylindrical chamber, the open extremity of which can be firmly pressed under an overhanging brow. This in a perfectly dark room will illuminate the region under which lies the frontal sinus, provided the sinus be of tolerable size and the walls correspondingly thin. If one sinus be full of pus and granulations it will appear less translucent than the other. But of course the method is of no value in the many cases in which both frontal sinuses are involved simultaneously.

The anterior ethmoidal cells sometimes open directly into the roof of the middle meatus, that is to say, into the concavity of the middle turbinal; at other times they may open into the lower part of the infundibulum. In the former case we are often able to pass a probe—and it should always be a blunt one—directly into the region in question; but in the latter case it is extremely difficult to detect the source of the discharge. Occasionally also these cells open directly into the antrum, and, it is said, into the orbit. After the persistence of the disease for any length of time, the floor and party walls of these little chambers become absorbed and break down, and granulation tissue fills up the cavities, into which the probe freely passes, discovering here and there spots of carious bone; and, as I have said before, ethmoidal mischief is frequently associated with like trouble in the antrum, infundibulum, and frontal sinus. The pus may even make its way directly into the maxillary sinus, into which the disease may also extend. Indeed, I have a suspicion that many cases of such extensive nose disease begin in a small abscess affecting an ethmoidal cell.

I have purposely said nothing about symptoms in frontal disease, seeing that, so far as I am aware, they are only with great difficulty to be distinguished from those of disease of the antrum. Probably supraorbital pain is even a commoner symptom; and I am inclined to think that periodicity in the flow of pus may be more frequent in the case of the frontal sinus. Thus cases occur where the patient, after taking cold, has attacks of "brow-ague" at variable intervals, such as one, two, or more days, which pain, after persisting with increasing intensity for some hours, is suddenly relieved by a copious flow of purulent secretion; and unless the patient present himself for examination during such a discharge, we may find no objective indication whatever of the nature of his ailment. Such symptoms are probably indicative of small spots of acute suppuration; and the very fact of their undergoing spontaneous recovery makes it impossible to determine whether an ethmoidal cell or the frontal sinus be concerned. We are altogether dependent on the patient's subjective experience. In either case one would assume that spontaneous recovery is more likely to occur than in antral disease.

Formerly, when a correct diagnosis was barely attempted, the treatment of such cases consisted in the removal of the larger masses of polypus and granulations; the patient was then dismissed with the consolatory advice that he was suffering from a chronic catarrh which would persist in spite of all treatment; or he was sent to Egypt or South Africa, the chief recommendation of such places being their distance. But now, with improved methods of diagnosis, practice has so far changed that, as regards ethmoidal disease at any rate, no difference of opinion will be found among specialists as to the importance and the success of treatment. Whether we are dealing with ethmoidal or frontal disease, the principle of treatment consists in securing free drainage; if this can be secured, we may entertain every hope that the suppurating cavities will gradually become obliterated by organising granulation tissue. In the case of ethmoidal cells the process can be greatly facilitated by cautiously breaking down the very friable dissepiments with a curette, which instrument is also most usefully employed in removing such granulation masses as are interfering with free drainage. The curette is preferable in every way to caustics, though doubtless these have their use when carefully applied and to small areas at a time. The electric cautery has only to be mentioned in words of condemnation; and we may lay it down as a rule that whenever the limitation of a polypus or granulation mass is indefinite, whenever we are unable to determine the actual distance from the cribriform plate at which we are working, the galvano-cautery ought never to be used. And it is this imperative necessity for caution in such operation, as it appears to me, that makes the treatment of these cases very tedious: yet after a few sittings the patient becomes so far convinced of the improvement in his symptoms that he is ready enough to undergo a prolongation of the treatment. In the case of the frontal sinus it is not easy to secure free drainage; but as, perhaps, the majority of such cases (and as far as my experience goes, I should say all of such cases) are complicated with suppuration in the infundibulum and its contributory cells, it is obvious that to open the sinus from the outside will not be altogether successful. This, of course, was formerly the routine procedure for acute abscess, and up to a certain point must still be admitted as correct; but in chronic cases, unless accompanied by intra-nasal treatment, it is far less satisfactory than drilling the antrum. Of late I have sought to abandon the external opening altogether, seeing that to the patient it is a serious operation, entailing a certain amount of disfigurement, and considerable distress in the after-treatment. My object has been to break down the inner walls of the infundibulum, often attenuated or partly destroyed by the disease, after removing the anterior extremity of the middle turbinal. The channel generally corresponds with a distinct bulging into the middle meatus; and into it a fine chisel or indeed a blunt raspatory can be easily thrust, and the inner wall broken away piecemeal. In this manner the passage can be laid open as far upwards and forwards as the anterior extremity of the attachment of the middle spongy bone, and an opening thus made sufficiently large to admit of easy irrigation, which, indeed, the patient can sometimes be taught to practise for himself. Once free drainage is secured, the natural tendency is to spontaneous cure by cicatrisation, and more or less to the obliteration of the cavity.

Posterior ethmoidal cells.—Every remark that has already been made concerning the etiology and pathology of suppuration in the anterior ethmoidal cells applies to the same affection of the posterior. The only difference is in diagnosis. But this is actually an easier matter with the posterior than the anterior, seeing that suppuration in the former is not so frequently associated and confounded with disease in the antrum and frontal sinus. The one point in diagnosis is that, in the case of the posterior cells, while the discharge flows by preference into the post-nasal space, it may occasionally pass through the anterior nares, when, on examination, it will be found occupying the space between the free border of the middle turbinal and the septum ; for, as will be remembered, the posterior ethmoidal cells open into the superior meatus, which is fully developed only in the posterior portion of the nasal cavity. On examining the posterior nares with the post-rhinoscope, the pus will be seen occupying the region of the superior turbinal, which may be wholly or partly obscured by polypus or by masses of less transparent and redder granulation tissue. Examination of this region with a probe is by no means easy owing to the obstructing middle turbinal; nor is the removal of the posterior extremity of this structure an altogether commendable operation. And even when this difficulty is surmounted, it may prove impossible to clear out the largest of the posterior ethmoidal cells, seeing that this cavity, extending outwards and backwards, is often of considerable size. And for similar reasons irrigation of the upper and back regions of the nose is extremely difficult to carry out satisfactorily.

Suppuration in the sphenoidal sinus.—Abscess of the sphenoidal sinus is, according to my experience, extremely rare; and in most of the recorded cases of so-called sphenoidal suppuration the clinical points, as related, have failed to convince me of the observer's sagacity in diagnosis. For my part, I have only been able to diagnose three cases positively. Acute abscess, like suppuration in the other cavities, is said to occur as the result of syphilis, tuberculous meningitis, erysipelas, and acute rhinitis. In acute abscess the symptoms described are intense deep-seated pain referred to the centre of the head; as the pain increases in severity, symptoms of pressure on surrounding parts supervene, the optic nerve is compressed, and sudden blindness follows. Exophthalmos and strabismus should be accompaniments; and where necrosis occurs, orbital abscess and meningitis may follow.

The only difficulty in diagnosis arises from the similarity in the symptoms of posterior ethmoidal and sphenoidal suppuration, seeing that in each case the discharge finds its way more readily into the posterior nares than from the anterior. In every unequivocal case of suppuration of the posterior ethmoidal cells which I have seen, the pus did not conspicuously flow over the posterior walls of the naso-pharyngeal cavity, which indeed could happen only when the patient was lying on his back. On the contrary, in a supposed case of empyema of the sphenoidal sinus, the pus would obviously flow over the posterior wall whether the head were held upright or supine; while the only position in which it could gain access to the nasal fossæ would be when the patient was lying prone:

yet an occasional bend of the head forwards might account for some of it finding its way on to the superior turbinal. Such points will be perfectly clear if the anatomical arrangement of these cavities is remembered: the posterior ethmoidal cells open immediately into the superior meatus, and the sphenoidal immediately behind the posterior nares, although approximately on the same level. Briefly, the tendency in sphenoidal suppuration is for the pus to flow downwards over the posterior wall of the naso-pharynx, keeping to the affected side of the middle line; while in posterior ethmoidal suppuration the pus, though flowing also backwards and downwards, finds its exit from both anterior and posterior nares, favouring the latter; the examination does not indicate that it is confined to the posterior naso-pharyngeal wall, unless the patient has been lying for some time upon his back.

The treatment, when the diagnosis is clear, consists in cautiously breaking down the anterior wall of the sinus, which, looking directly forwards and sometimes slightly downwards, is readily reached by passing the instrument upwards and backwards through the anterior nares, and following the line of junction of the perpendicular plate of the ethmoid with the vomer. But it must always be remembered that the size of this sinus varies greatly.—G. MACD.

Naso-pharyngeal or post-nasal catarrh.—**Acute catarrh** of the naso-pharynx is usually associated with a similar condition of the nose and pharynx. It is accordingly seen in cases of measles and scarlet fever, typhoid fever, and other infectious diseases which attack the nose and throat. The symptoms and treatment are the same as for acute nasal and pharyngeal catarrh.

Chronic catarrh of the naso-pharynx is most commonly due to some obstruction to free nasal respiration, as for example deflection of the septum, or crests on it, hypertrophic rhinitis, and especially enlargement of the posterior extremity of the inferior turbinals, or the presence of polypi. In some cases chronic enlargement of the pharyngeal tonsil seems to be the direct cause; and Tornwaldt laid great stress on the so-called pharyngeal bursa as the seat of the processes leading to catarrh of the naso-pharynx. Recent researches, however, have shown that this bursa is only the remains of the normal median cleft in the pharyngeal tonsil. Naso-pharyngeal catarrh is often accompanied by gastro-intestinal disturbance, and treatment of the latter will relieve the former.

The *symptoms* of naso-pharyngeal catarrh are those due to obstructed nasal respiration with increased secretion. The patient usually wakes in the morning with the mouth dry; he feels a sense of discomfort in the back of the nose, which is relieved by hawking and clearing the throat. There is frequently some laryngeal catarrh as revealed by hoarseness. Owing to the Eustachian tubes becoming blocked by catarrhal swelling of their mucous lining, complaint is made of deafness and of tinnitus aurium; otitis media sometimes occurs. Headache, pains in the nape of the neck, and giddiness are not uncommon symptoms. On examination of the naso-pharynx by means of the rhinoscope the mucous membrane will be found swollen and usually more or less covered with sticky mucus or dry crusts. Occasionally enlargement of the pharyngeal tonsil may be detected. In the more chronic cases atrophic changes, similar to those seen in atrophic rhinitis, may be recognised. The nose should be carefully examined in order to detect any obstructive lesion.

Treatment.—In the milder cases tonics, change of air, and attention to the state of digestion will usually have a good effect. If the symptoms continue in spite of this method of treatment, the use of mild alkaline solutions to the nose and naso-pharynx by means of the anterior or posterior spray will yield beneficial results, especially if followed by spraying the parts with a solution of twenty grains of menthol and fifteen minims of eucalyptol in an ounce of fluid paraffin. In cases in which the pharyngeal tonsil seems to be the seat of the mischief, the application of a solution of ten grains of iodine and twenty of iodide of potassium and five minims of oil of peppermint in an ounce of glycerine by the post-nasal brush, night and morning, will have an excellent effect. If the pharyngeal tonsil is much enlarged it may be necessary to remove it by means of the curette or forceps.

Should the catarrh be dependent on nasal obstruction, free nasal respiration must be secured by surgical treatment adapted to the special necessities of the individual case.

Tuberculosis may attack the naso-pharynx, giving rise in some cases to ulceration, and in others to a diffuse infiltration of the posterior aspect of the soft palate. Tubercle bacilli have been detected in adenoid vegetations.

Syphilis in all its forms has been observed in the naso-pharynx. Primary syphilis of the naso-pharynx is almost exclusively due to infection by means of the Eustachian catheter.

Secondary syphilis occurs in connection with a similar affection of the pharynx.

It is not at all uncommon for tertiary ulceration of the naso-pharynx to occur quite independently of any mischief in the pharynx, hence the importance of a rhinoscopic examination in these cases.—F. DE H. H.

Hypertrophy of the pharyngeal tonsil.—*Adenoid vegetations; Post-nasal growths.*—The aggregation of lymphoid tissue on the roof and posterior wall of the naso-pharynx, known as the pharyngeal or Luschka's tonsil, is very similar in structure and formation to the faucial tonsils, and is liable to the same morbid changes. In fact, in about 50 per cent of the cases hypertrophy of the faucial tonsils and post-nasal adenoids co-exist; but the latter disease gives rise to a distinctive group of symptoms, the clinical importance of which, first recognised and described by Wilhelm Meyer of Copenhagen in 1868, is becoming very generally appreciated.

Etiology.—Post-nasal adenoid hypertrophy is a disease of early childhood, a period when all the lymphatic structures are, especially active. It has been observed as early as the tenth month; the symptoms generally date from birth or early infancy, becoming well marked, as the hypertrophy increases, by the fourth or fifth year, if not before. Thus there is little room for doubt that the affection is often congenital in origin. The majority of cases come under our notice between the ages of five and fifteen; and the adenoids, though sometimes persisting and still more rarely extending after the age of twenty, in nearly all cases participate in the retrogressive changes and atrophy common to many lymphatic structures after the age of puberty. By this time, however, the health and development of the patient are often permanently impaired.

The considerable influence of heredity in their occurrence is shown by the frequency with which several members of a family suffer from adenoids. This influence is probably indirect, and is due to the transmission of the strumous diathesis in which we observe so marked a tendency to hypertrophy, and degeneration of the lymphatic glands and a decided proclivity to tuberculous affections. Further, we often find, associated with the rhino-pharyngeal affection, various inherited defects in development, such as a high-arched or V-shaped palate, contraction of the superior maxilla and consequent encroachment on the nasal fossæ and cleft palate. The importance of nasal stenosis as an etiological factor in producing the adenoid hypertrophy has been over-estimated: nasal stenosis and chronic nasal catarrh are almost always the results of post-nasal growths and concomitant defects in development.

A cold and damp climate disposes to the disease by increasing the tendency to catarrhal affections; and in warm and dry climates the disease is less common: thus Massëi remarks that in Italy the disease is very rarely observed in any marked degree. Measles, scarlatina, and influenza are apparently very frequent exciting causes of the disease. On the other hand, it is equally certain that the presence of adenoids very greatly increases the risk of infection in various exanthems, and the liability to colds and bronchitis; thus it is often very difficult here to distinguish between cause and effect. Finally, in many patients who are otherwise healthy and strong we find no obvious cause for the glandular hypertrophy.

We have no certain knowledge of the physiological functions of the lymphoid tissue in the upper air-passages; but it is probable that they furnish leucocytes which are protective against the inspired micro-organisms that always exist in these parts. This question is more fully discussed in the chapter on the diseases of the tonsils. But it is quite certain that the pharyngeal tonsil, when in a condition of chronic hypertrophy and degeneration, like all tissues of low vitality, has lost its power of resisting the invasion of pathogenetic microbes, and is a ready portal of entrance for tubercle bacilli. Thus the pharyngeal and particularly the cervical lymphatic glands are frequently affected and become enlarged in cases of adenoid vegetations, and one of us (F. S.) has twice of late seen retro-pharyngeal abscess associated with adenoids.

Pathology.—The growths occupy the vault and posterior wall of the rhino-pharynx, forming either a large cushion-like mass or an aggregation of numerous large and irregular projections. They are covered with ciliated epithelium and the surface is coarsely lobular or mammillar. The substance of the growths consists of a connective-tissue reticulum filled with lymph corpuscles, the trabeculæ being formed of ramified corpuscles which have generally lost their nuclei. The tissue is, as already mentioned, very similar to that of the faucial tonsils, differing only in the absence of the crypts, the relatively small amount of connective tissue, the high vascularity, and the ciliated epithelium. Tuberculous tissue has been observed in the vegetations, and, very rarely, small cysts also. In adult patients we generally find the growths more or less atrophied, and firmer in texture from the preponderance of connective tissue.

The symptoms vary very much in kind and in severity: thus while in some cases there is little to observe but nasal obstruction or deafness, in the vast majority the symptoms are so characteristic that the general aspect alone is sufficient for the practised eye to make a diagnosis of post-nasal growths. The nose becomes pinched, the alæ nasi fall in from long-continued disuse of the dilator muscles, and a dimple forms in the angle between the superior and inferior lateral cartilages. The upper lip is retracted, the upper incisors show, the naso-labial fold is more or less obliterated, and, the inner canthus of the eye being drawn down, the eyelids droop and the whole face lengthens; moreover, the necessity of breathing through the mouth gives an expression of dulness and vacuity which is still further increased by deafness. The child is generally pale and unhealthy-looking, and the cervical lymphatic glands are often enlarged.

Defective growth and all the evils due to mechanical obstruction to respiration in the young are often observed; as, for instance, chronic pharyngitis, colds in the head, laryngitis, and bronchitis. Dr. Eustace Smith, whose experience of diseases of children is exceptionally wide, observes that in childhood symmetrical retraction of the infra-mammary region and depression of the ensiform appendix (pigeon-breast) owe their origin with few exceptions to rhino-pharyngeal obstruction, the retraction of the chest wall being directly due to pulmonary collapse. If this collapse be extensive, the lower part of the sternum becomes prominent from retraction of the cartilages of the ribs, whilst the recession of the infra-mammary and epigastric regions with each inspiration, noticed in very young children suffering from rhino-pharyngeal obstruction, results, if long continued, in permanent retraction of these parts. Moreover, in infants and young children with adenoids it is common to find collapse of the upper parts of the lungs; and there may be deficient resonance with weak, harsh breathing in the supraspinous fossæ, extending down to a short distance below the scapular spine: this may be accompanied by a dusky tint of the lips with other signs of imperfect aeration of the blood. Dr. Smith reminds us that, at this period of life, a high-pitched percussion note in the supraspinous fossæ, without notable alteration in the breath sounds, is commonly due to a patch of pulmonary collapse; and that when the rhino-pharynx is obstructed by a mass of adenoid growths, very hollow breathing, conducted from the pharynx, is heard over the upper part of the chest on either side—a combination of physical signs which often leads to an erroneous diagnosis of serious disease.

The breathing of children suffering from advanced adenoid vegetations is peculiarly noisy and snuffling; this is very noticeable during eating and drinking, and especially in sleep. While in the daytime respiration is mainly by the mouth, the physiological habit of nasal respiration reasserts itself during sleep; moreover, the tongue tends to fall back against the soft palate, by which respiration is still further embarrassed, and snoring is set up. Suffocative "night-terrors" often occur; the little patients are always restless in bed and their sleep much disturbed: for as the embarrassed respiration through the nose creates an excess of carbonic acid gas in the blood, the *besoin de respirer* arouses the child so far as to take a few breaths by the mouth.

Speech is affected as the nasal obstruction interferes with the pronunciation of certain consonants: thus B is substituted for M, D for N, G for NG and K, F for TH, and so forth. The voice is also remarkably toneless and flat, since the rhino-pharynx, being occupied by the growths, loses its resonant functions. Apart from these effects of nasal obstruction the children are usually backward in learning to speak and read; and articulation is very often defective, partly from want of tone in the palate muscles, and partly from deafness. To the deficient aeration of the blood must further be ascribed the lassitude, the "ready flagging," the headaches and giddiness of the little patients, and their inability to fix their attention (Guye's "aprosexia").

A peculiar harsh, dry, barking, reflex cough, independent of any bronchitic affection, is a very frequent complaint; it is usually worse at night. Cough is further induced by the accumulation of mucus in the back of the throat trickling down to the larynx, or by catarrhal affections of the upper respiratory tract. The soft vascular adenoids bleed so readily that the secretion is often blood-stained; and blood, even in considerable quantities, may be coughed up or, passing into the stomach, may be vomited. Whilst a history of inveterate cold-taking with constant running from the nose is usual, yet, on the contrary, the complaint may be that the child has a particularly dry nose, and that he never uses a pocket-handkerchief; although his speech sounds as though he has a cold in his head. Asthma, stuttering and stammering, laryngismus stridulus, chorea, nocturnal enuresis, and even convulsions and epilepsy, are among the neuroses that have been attributed to the presence of adenoids. Though we should guard against the tendency to refer every conceivable reflex neurosis to a rhinal or rhino-pharyngeal irritation, it is conceivable that adenoids may cause any of these symptoms; and we have strong evidence of the intimate association between the upper and lower respiratory tract in the fact that respiration may be completely arrested by the presence of the forefinger in the rhino-pharynx. Probably the intensely disagreeable sensation of choking produced by digital exploration of the rhino-pharynx for diagnostic purposes, arises largely from the same cause.

Deafness in greater or less degree—sometimes periodical and coincident with cold in the head, sometimes constant—is one of the most frequent complications of adenoids; although very often treated lightly by the parents, who trust that the child will grow out of it; or they regard it as mere "inattentiveness." From the gradual absorption of the air in the middle ear which cannot be renewed—either in consequence of the Eustachian tubes becoming obstructed by catarrh in the naso-pharynx, or from paresis and interference with the action of the levator palati and salpingo-pharyngeus muscles—the tympanic membranes become so much depressed that on examination we see extreme foreshortening of the handle of the malleus, prominence of the short process and posterior fold, and an ill-defined or absent bright spot. The membrane is often thickened and somewhat opaque and congested. From retention of the catarrhal secretions otitis media purulenta may arise with subsequent perforation, otorrhœa, and granulations. The extreme degrees of depression of the drum-heads are practically never seen in children except in connection with adenoid vegetations. Should a child suffering from adenoids be attacked by scarlet fever or diphtheria, ear-complications, often severe and even incurable, are almost the rule.

In adults, the growths having usually become more or less atrophied while the rhino-pharyngeal space has increased, nasal obstruction and mouth-breathing generally disappear; though many of the evil effects persist.

On examining the fauces the soft palate is seen to be relaxed, and its distance from the posterior wall of the pharynx unusually great. If the tonsils are not greatly hypertrophied, as in these cases they often are, numerous enlarged follicles on the posterior wall of the pharynx may be seen, unless they are obscured by the muco-purulent secretion descending from the rhino-pharynx. The growths themselves may be examined by rhinoscopic inspection and by palpation. Even in very young children it is occasionally possible to obtain a view of the rhino-pharynx with the rhinoscope. The growths appear either as a grayish pink gelatinous cushion-like mass with vertical ridges and furrows, or as an aggregation of stalactite-like projections crowded together and presenting an irregular mammillated surface growing from the vault and posterior wall. They often extend laterally to the fossæ of Rosenmüller, or occlude the orifices of the Eustachian tubes more or less, sometimes forming adhesions with the posterior lips. The Roman arch formed by the upper insertion of the vomer into the roof of the naso-pharyngeal cavity and the choanæ are partially shut off from view; or the whole rhino-pharyngeal space may be filled with masses of growth. The surface of the mass is often more or less covered by viscid muco-purulent secretion. In adult patients it is not difficult to make the rhinoscopic examination.

Digital exploration of the rhino-pharynx should be employed in all doubtful cases. With the child seated in a chair, the physician standing on the right side and holding the head firmly with the left hand, the right forefinger, protected either by a finger-guard, or by a napkin, or by a cork between the patient's teeth, is rapidly passed behind the posterior pillar of the fauces, and thence upwards to the roof of the rhino-pharynx, and swept rapidly over the whole of the post-nasal space so as to determine the size, consistency, and location of the vegetations. As the forefinger impinges on the soft adenoids, the sensation reminds one of a bag of worms. However gently and carefully the examination be made, there is almost always some bleeding, and on withdrawing the finger it is stained with blood. Disagreeable though the digital exploration be, we must not be deterred from employing it, unless the posterior rhinoscopic examination yields absolutely satisfactory results; indeed, palpation is superior to the latter method in enabling us to form a definite notion of the quantity of the growths present.

Diagnosis.—It is only in infants or very young children, whose undeveloped features do not show the characteristic facial aspect described above, that a difficulty in diagnosis should be possible. Nasal discharge and snuffling respiration, which as we have seen are marked symptoms in adenoid cases, are also frequently associated with congenital syphilis. But in syphilitic infants the nostrils are dry and show radiating linear fissures; and, nasal obstruction being more complete, they are unable to take the breast. Moreover, other signs of the constitutional disease are usually present. Other kinds of growth in this region are extremely rare in children. In adults a differential diagnosis may have to be made between persistent adenoids, fibroma, nasal polypi extending backwards from the nose, and moriform hypertrophy of the inferior turbinals; all of which, with the exception of nasal polypus, are extremely rare conditions, and may readily be distinguished by the seat of origin, colour, or consistency.

Prognosis.—The prognosis is always favourable on the whole, provided no serious complication have arisen; broadly speaking, it stands in direct proportion to the patient's age and to the length of time the obstruction has existed. The most brilliant results are obtained by timely operation in young children; but the prospect, of course, is less favourable if organic changes have once taken place in the middle ear, or thoracic deformities are definitely established, or the time has passed when, by relief of the obstruction, an advantageous change could be expected in the configuration of the face. Although the adenoid growths, as a rule, atrophy spontaneously after puberty, and, with the increasing size of the rhino-pharyngeal space, the symptoms usually disappear, yet, before that age is attained, not only does a child run great risks of permanent deafness and impaired health and development, but it is also constantly exposed to attacks of catarrh and bronchitis, and is increasingly liable to contract the various exanthems. Moreover, in a certain number of cases the spontaneous atrophy is very partial; in others the symptoms do not vanish with the disappearance of the growths: whereas by skilful and timely treatment the whole disease can be completely and permanently eradicated and all these risks to health removed. Children almost invariably show a most remarkable improvement in general health and intellectual development within a short time of the operation; the pale and dusky complexion and dull woe-begone expression are replaced by brightness and intelligence, healthy respiration dilates the lungs, the chest develops, and the patient increases in stature, weight and activity. In short, removal of adenoids in really suitable cases is one of the greatest medical blessings of our era, and must have a far-reaching effect upon the health of future generations!

Our advice should be as follows:—If the patient be under twelve, while certainly admitting that the child may escape all the dangers involved in the disease, yet all the disadvantages of postponement may be removed by an operation which, if properly and skilfully performed, is practically devoid of danger. Of course no unnecessary operations should be performed, but in doubtful cases it is better to operate. We must not definitely promise that the growths will not recur, for even after very thorough and complete extirpation recurrence takes place in a small percentage (in our experience amounting to 1 per cent), especially after influenza. Moreover, some of the symptoms, especially speech defects, may persist for a considerable time after treatment.

Treatment.—Unless the vegetations be very small, and not productive of any of the more serious symptoms above enumerated, no time should be lost in internal medication or change of air. Whilst again deprecating unnecessary operative interference, one of us (F. S.) must confess that more than once in the light of subsequent events he has regretted that, guided by the wish to spare the patient an operation which at the time did not seem to be urgently required, he had not laid more emphasis on the risks of delay. Moreover, there cannot be the least doubt that the operation itself acts indirectly as a powerful tonic, and promotes the desired restoration to health more effectually than any amount of cod-liver oil, extract of malt and iodide of iron.

Operative treatment is called for in the great majority of cases presenting definite symptoms, and the younger the child the greater the reason for removing the growths without delay. For their complete extirpation a general anæsthetic ought to be employed, at any rate in children, and though in adults removal may be done under cocaine, a general anæsthetic is desirable. We give chloroform only for this operation. There is practically no risk with this anæsthetic, provided it be given slowly and cautiously, and not pushed to the abolition of the cough-reflex, which protects the larynx against the entry of blood. Fortunately it has been shown, by Semon and Horsley, that this reflex is the last to go; and the administration of the anæsthetic should therefore cease as soon as the conjunctiva is insensitive. If possible, no further anæsthetic should be given after the operation is once begun. The advantage of chloroform over gas and ether is that the latter combination gives a very short time for operating, while ether alone increases the vascularity of the parts, induces a copious secretion of frothy mucus, and is not so well borne by young children disposed to bronchitis. We quite admit that it is possible to remove both tonsils and adenoid growths under nitrous oxide gas alone; but in our opinion there is less opportunity for a complete removal of the growths, and a greater likelihood of recurrence, than when the operation is somewhat more deliberately performed under chloroform; and whenever operative interference is undertaken, the importance of a thorough and radical removal cannot be over-estimated.

As regards the particular method of removing the growths there is wide choice. Some operate by scraping with the finger-nail, others by curetting with post-nasal cutting curettes introduced through the mouth; or with a straight curette as employed by Meyer through the anterior nares; or by the use of cutting forceps, such as Loewenberg's; or by snaring with the cold or galvano-caustic wire, and destruction by caustics or the galvano-cautery. Each of these methods has its advocates, nor can the surgeon confine his practice to any one method.

Our own practice is to have the patient lying on his back with the head well extended and low down, a small pillow being placed under the neck. The mouth being kept open by a gag on the left side, held by an assistant, the operator, standing on the patient's right, passes a Gottstein's curette behind the soft palate to the vault of the pharynx, and then while gently but firmly pressed against the posterior wall it is drawn down so as to cut away the whole mass of growth, which, appearing below the soft palate, is readily removed by aseptic sponges attached to long straight holders. If vegetations are situated laterally in Rosenmüller's fossæ, these are removed in a similar manner with Hartmann's curette. The right forefinger is then introduced, and rapidly swept over the vault into the fossæ of Rosenmuller and over the Eustachian orifices, ascertaining whether anything has been left behind, and scraping away, if necessary, any remnants of growth with the finger-nail. The curette has often to be introduced several times. Hæmorrhage is always very free for a few minutes, but soon ceases spontaneously. Secondary hæmorrhage is exceedingly rare; in our experience it has never happened: cases, however, have been reported in which it was necessary to plug the rhino-pharynx. If the tonsils are hypertrophied and demand removal, this is done by us after the adenoids have been operated on; except in cases where the tonsils are enormous and impede the administration of the anæsthetic or the removal of the adenoids, in which case they should be removed before the adenoids.

For tough growths we find it necessary in very rare cases to use cutting forceps, such as Loewenberg's. With the left forefinger in the rhino-pharynx the forceps are guided to the portions of growth to be removed, care being taken not to include mucous membrane or any of the normal structures.

The after-treatment is very simple; the patient is kept in bed for twenty-four hours, and fed on cold bland food, such as milk, custard pudding, beaten-up eggs, and jelly. The temperature is sometimes slightly febrile the first night, and the throat rather sore; but this is very transitory and slight, and is relieved by sucking ice. The bowels should be well moved. The next two days the patient is confined to his bedroom, and for two days more to the house. No cleansing of the parts is necessary or advisable. A nasal or post-nasal douche should never be employed, as there is great risk of setting up otitis media by their use. Since giving up cleansing of the parts, and all after-treatment of the rhino-pharynx, we have hardly ever seen otitis media. For the first two or three days, owing to the irritation and inflammation set up by the operation, the nasal obstruction and deafness may be but little improved.

As regards the ears, if the membrane be simply depressed, it may suffice to inflate the middle ear by means of Politzer's bag; or, that failing, by the Eustachian catheter, for a variable period. This should not be undertaken till nearly a week after the removal of the growths, lest any blood, muco-pus, or disintegrating tissue be driven into the Eustachian tubes. But with middle ear disease the prognosis must be guarded, especially if perforation of the drum-head and chronic otorrhœa be present—serious complications which require their appropriate treatment. The nasal catarrh usually subsides in the course of a week or ten days.—F. S. and W. W.

REFERENCES

1. Ball, J. B. *Diseases of the Nose and Pharynx.* London, 1894.—2. Beiger and Tyrman. *Die Krankheiten der Keilbeim-Hohler und des Siebein-Labyrinthes.* Wiesbaden, 1886.—3. Billroth. *Ueber den Bau der Schleimpolypen.* Berlin, 1855.—4. Blackley, C. H. *Hay Fever: its Causes, Treatment, and Effective Prevention.* London, 1880.—5. Blake. "Relation of Adenoid Growths in the Naso-pharynx to the Production of Middle-Ear Disease in Children," *Boston Med. and Surg. Jour.* March 15, 1888.—6. Bosworth. *Diseases of the Throat and Nose.* New York, 1897.—7. Bresgen. "Der Circulationsapparat in der Nasenchleimhaut vom klinischen Standpunkt betrachtet," *Deut. med. Woch.* 1885, Nos. 34, 35.—8. "Discussion on Atrophic Rhinitis," *Trans. Internat. Med. Congress*, 1881, vol. iii.—9. Frankel, B. "Ueber adenoide Vegetationen," *Deut. med. Woch.* 1884, No. 41.—10. Freudenthal, W. "Rhino-scleroma," *New York Med. Jour.* Feb. 1, 1896.—11. Grunwald. *Die Lehre von den Naseneiterungen.* Munchen, 1896.—12. Guye, Luc, Zuckerkandl, M'Bride, and others. "Discussion on the Etiology of Mucous Polypi of the Nose," *Brit. Med. Jour.* 1895, vol. ii. p. 474 *et seq.*—13. Hall, F. de Havilland. "Epistaxis," *Westminster Hospital Reports*, vol. viii.—14. *Idem. Lettsomian Lectures*, 1897.—15. *Idem. Diseases of the Nose and Throat.* London, 1894.—15*a*. *Idem.* "On Diagnosis and Treatment of Empyema of the Nasal Accessory Sinuses," *Brit. Med. Journ* 15th December 1894, p. 1358.—16. Heath, Christopher. "On certain Diseases of the Jaws," *Hunterian Lectures*, 1887.—17. *Idem. Injuries and Diseases of the Jaws.* London, 1894.—18. Heaven, J. C. "Fibrinous Rhinitis or Diphtheria," *Public Health*, vol. viii. No. 7.—18*a*. Heryng. "Die electrische Durchleuchtung der Highmorshohle bei Empyem," *Berlin. klin. Woch.* 1889, Nos. 35, 36, p. 798 *et seq.*—19. Hulke, J. W. "Five Cases of Disorders of the Frontal Sinuses," *Lancet*, 1891, vol. i. p. 589.—20. Kjellmann. "Epileptiform Convulsions dependent on intra-nasal Changes," *Hygeia.* Stockholm, Feb. 1893.—21. Knight, C. H. "Nasal Sequelæ of Syphilis and their Treatment," *Trans. Amer. Laryng. Assoc.* 1896.—22 Loewenberg. *Tumeurs adénoides du pharynx nasal.* Paris, 1879.—23. *Idem.* "Les végétations adénoides dans la vaûte du pharynx," *Trans. Internat. Med. Congress*, London, 1887.—24. M'Bride, P. *Diseases of the Throat, Nose, and Ear.* Edinburgh, 2nd edition.—25 M'Bride and Logan Turner. "Naso-Pharyngeal Adenoids: a Clinical and Pathological Study," *Edin. Med. Jour.* new series, vol. i. 1897.—26. Macdonald, Greville. *Diseases of the Nose.* London, 1892.—27. Mackenzie, Morell. *Diseases of the Throat and Nose*, vol. ii. London, 1884.—28. *Idem. Hay Fever and Paroxysmal Sneezing* London, 1887.—29. Mackenzie, J. N. "The Pathological Anatomy of Strumoid Disease," *Trans. Amer. Laryng. Assoc.* 1896.—30. Major. "Lupus, Tuberculosis, Syphilis, Glanders, and Diphtheria of the Nose and Naso-pharynx," Barnette's *System*, 1893.—31. Mayo-Collier. "Deflections of the Nasal Septum," *Jour. of Laryng.*

1891, vol. v.—32. Meyer, Wilhelm. "Adenoid Vegetations in the Naso-pharyngeal Cavity," *Med.-Chir. Trans.* vol. liii.—33. Nasal Obstruction, Discussion on, opened by Dundas Grant, *Brit. Med. Jour.* 1888, vol. ii. p. 602.—34. Newman, David. *Malignant Disease of the Throat and Nose.* Edinburgh, 1892.—35. Onodi. *An Atlas of the Anatomy of the Nasal Cavity and its Accessory Sinuses.* Translated by St. Clair Thomson. London, 1894.—36. Pierce, Norval. "Syphilis of the Nose," *New York Med. Jour.* Nov. 30, 1895.—37. Roe, J. O. "Ætiology of Deviations, Spurs, and Ridges of the Nasal Septum," *Trans. Amer. Laryng. Assoc.* 1896.—38. Thomson, St. Clair, and Hewlett, R. T. "The Fate of Micro-organisms in Inspired Air," *Lancet,* Jan. 11, 1896.—38*a*. Voltolini. *Die Krankheiten der Nase Nachtrag.* p. 465 *et seq.* 1888.—39. Walsham, W. J. "On Nasal Obstruction and its Treatment," *St. Bartholomew's Hospital Reports,* vol. xxiii.—40. Watson, Spencer. *Diseases of the Nose.* London, 1890.—41. Watson Williams, P. *Diseases of the Upper Respiratory Tract, the Nose, Pharynx, and Larynx.* Bristol, 1897.—42. Zuckerkandl. *Anatomie der Nasenhohlen.* Wien, 1882.—43. *Idem.* *Normal und pathologische Anatomie der Nasenhohlen.* Wien, 1882.—44. *Idem.* "Schwellgewebe der Nasenschleimhaut und dessen Beziehungen zum Respirationsspalt," *Wien. med. Woch.* 1884, vol. xxxiv. No. 38.

II.—DISEASES OF THE PHARYNX

Pharyngoscopy:
Acute } Pharyngitis:
Chronic }
Hæmorrhage:
Diseases of the Uvula:—Felix Semon and Watson Williams.
Throat Affections of the specific febrile Diseases. F. de Havilland Hall.
Acute septic Inflammations of Pharynx and Larynx:
Retropharyngeal Abscess:
Pharyngomycosis Leptothricia:
Tuberculosis:
Syphilis.
Gout:
Rheumatism:
New Growths:
Neuroses:
Foreign Bodies in the Air and upper Food Passages:
Diseases of the Tonsils.—Felix Semon and Watson Williams.

Pharyngoscopy.—The pharynx and fauces may be examined by direct inspection in bright daylight, or by the aid of artificial light reflected and concentrated by a forehead mirror, which should be the same as that used in laryngoscopy. The remarks on the form of the forehead mirror and the best kind of light will be found on page 780.

In examining the pharynx, we sit facing the patient with the forehead reflecting mirror over the right eye, so adjusted that the eye looks through the aperture in the centre. The lamp, if one be used, should be placed on the patient's left, on a level with his ear, and so that the light is directed towards the forehead mirror and thence into the patient's mouth.

The patient should then open his mouth and go on breathing quietly, when in many cases a good view of the fauces will be obtained; generally, however, it is necessary to depress the tongue with a spatula or some form of depressor, such as Turck's or Frankel's. In introducing the depressor it should be placed just beyond the dorsum of the tongue, and then gently and steadily depressed. If not far enough back, the dorsum of the tongue bulges up and impedes the view; on the other hand, if it is placed too far back, retching and nausea are induced. If the tongue is forcibly arched up, gentle pressure should be continued for a moment, if we attempt to depress the organ forcibly, it will arch up the more.

In the first place, the condition of the parts during quiet respiration should be noted. The tonsils are seen lying between the anterior and posterior pillars of the fauces; they should not project beyond the faucial pillars. Behind the faucial opening the posterior wall of the pharynx comes into view. The colour and surface of this part and of the soft palate should be noted. The patient should then be instructed to sound "Ah! ah!" and the power of retraction of the velum palati observed.

A laryngeal mirror ought then to be introduced as in laryngoscopy; but the mirror should be held less obliquely, so as to reflect the back of the tongue and the upper surface of the epiglottis; by this means we observe the condition of the lingual tonsil. Simple enlargement and tortuosity of the superficial veins at the back of the tongue are very common, and are devoid of clinical importance. The lower portion of the pharynx and the beginning of the œsophagus are seen by placing the mirror in the position for laryngoscopy, while the patient's tongue is protruded and held by a cloth in the examiner's left hand Finally, the back of the uvula and soft palate, and the rhino-pharynx should be examined with the rhinoscope, as in posterior rhinoscopy.

The rhino-pharynx is continuous with the anterior nasal cavities, and extends from the base of the occiput and sphenoid downwards as far as the isthmus, the narrow space corresponding to a line drawn from the posterior margin of the soft palate to the posterior pharyngeal wall Into it open the Eustachian tubes by trumpet-shaped orifices, from the posterior margins of which may be seen the salpingo-pharyngeal folds extending downwards, and forming on each side a fossa between themselves and the posterior wall of the pharynx—the fossa of Rosenmuller. The orifices of the Eustachian tubes are just behind the posterior extremities of the inferior turbinated bodies.

The mucous membrane is covered with ciliated columnar epithelium, and is more abundantly supplied with mucous glands than the anterior nasal cavities. Numerous lymphoid follicles exist throughout the pharynx; and a collection of these in the roof and posterior wall of the rhino-pharynx forms a mass, similar to the faucial tonsils, named Luschka's, or the pharyngeal, tonsil. The pharyngeal tonsil presents an uneven surface with longitudinal ridges. At the lower extremity is the elevated bursa pharyngea, with its central depression—the "foramen."

The colour and condition of the various structures must be carefully noted. Some departure from the usual smooth, pinkish red character of the mucous membrane of the pharynx must be regarded as within the limits of the normal; for, as in the nose, it is important not to diagnose every variation from the ideal pharynx as disease. Isolated anæmia of the pharynx and larynx, however, in patients otherwise not particularly anæmic, may possibly be a premonitory sign of tuberculous disease. Further, we must guard against overlooking any diseased condition on the posterior surface of the soft palate; for, particularly in syphilis, extensive infiltration and ulceration may affect its posterior surface only, without there being anything strikingly abnormal anteriorly, beyond some hyperæmia or defective mobility.

In cases of nerve disease it is necessary to use a probe to test the tactile sensibility and reflex irritability of the soft palate.

Finally, it is sometimes desirable to make the patient "gag," by introducing the tongue depressor rather farther back than usual, as in this way we cause the pharyngeal muscles to contract and to bring the tonsils well into view; thus sometimes considerable hypertrophy of these structures may be revealed, or such thickening of the lateral pharyngeal walls as we find in pharyngitis lateralis and in gouty pharyngitis.

Congenital malformations are occasionally met with; the most common being a more or less completely bifid uvula, or complete absence of the uvula in association with cleft palate. The anterior pillars of the soft palate may have a separate and complete fold of mucous membrane covering the palato-glossus muscle, with a perforation of the mucous membrane of the anterior pillars of the fauces which may be mistaken for perforation resulting from former disease.

An accessory thyroid gland has also been recorded, which formed a small tumour in the region of the lingual tonsil.

In conclusion, we cannot too strongly insist on the importance of paying attention to the general condition of every patient who consults his medical adviser for a throat affection. A chronic pharyngitis may arise from cardiac valvular disease, while gout, rheumatism, anæmia, and dyspepsia are prolific causes of acute and chronic pharyngitis; again, congestion of the pharyngeal mucous membrane and hæmorrhage from rupture of small vessels may be due to chronic renal disease, mitral stenosis, or portal obstruction.

Acute Catarrhal Pharyngitis.—The causes may be classified as follows:—(i.) *Idiopathic*, due to sudden exposure to cold and damp, especially after being in heated rooms; (ii.) *Diathetic*, especially gouty and rheumatic—many of the cases of so-called simple catarrhal pharyngitis, following exposure to damp, belong to this class; (iii.) *Toxic*, due to the action of various drugs, as, for example, antimony, mercury, belladonna; or to the virus of infectious diseases; (iv.) *Traumatic*, from burns, scalds, external violence, and the like.

Pathology.—How cold and damp may cause acute angina is uncertain; but acute catarrhal pharyngitis is frequently epidemic and often contagious, especially in the spring and autumn; this prevalence points to a microbial origin of many forms of acute catarrhal angina hitherto regarded as idiopathic and due directly to cold, and recent bacteriological researches corroborate this view. The very intimate connection between pharyngitis, acute tonsillitis, and the rheumatic diathesis, the fact that all these affections are prone to occur under similar climatic and telluric conditions, and also that acute tonsillitis and rheumatism are probably due to infection by micro-organisms, favour the view that the idiopathic and rheumatic forms of pharyngitis and acute rheumatism stand in much the same relation to one another as does the sore throat which prevails during epidemics of scarlet fever to scarlet fever itself.

On the other hand, there is no reason to believe that the toxic forms of acute pharyngitis are in any way associated with micro-organisms; they are more probably due to bio-chemical alterations in the tissues, similar to those resulting from the action of belladonna in acute poisoning by this drug.

Whatsoever the exciting cause of the inflammatory condition, the pathological changes in the pharynx are identical, and consist at first in general hyperæmia and round-celled infiltration of the affected region, with diminished secretion from the mucous glands, giving place in the course of twelve to twenty-four hours to increased secretion of grayish, viscid mucus which soon becomes muco-purulent. The implicated mucous membrane appears red, velvety, and thickened, and the uvula especially is prone to be thickened, elongated and œdematous. As the inflammatory condition subsides, the mucous membrane generally regains its normal colour and functions; but, on the other hand, a subacute catarrhal inflammation may persist for a considerable time, and in the absence of appropriate treatment may eventually pass into the chronic form.

The *symptoms* vary in degree according to the severity of the attack; in many cases they are slight and the patients do not seek advice. In the earlier stages a dry soreness in the throat is felt, especially during speaking or swallowing, with a sensation of stiffness in the parts, rendering speech uncomfortable. When resulting from a chill there may be some aching in the limbs and back, general malaise, and slight feverishness. The dryness and harshness of the throat are due to the arrest of the secretions; after a day or two a small quantity of tenacious purulent mucus is secreted; but this is rarely so excessive in amount as in chronic pharyngitis. The tonsils and uvula are generally more or less implicated, and are red and swollen, or in the severer cases dusky purple in colour; the catarrhal inflammation often spreads up to the rhino-pharynx, perhaps to the Eustachian tubes, giving rise to temporary deafness; or it passes downwards to the larynx and trachea.

Diagnosis.—It is necessary to bear in mind that diphtheria, scarlet fever, measles, and septic inflammations may begin with symptoms of acute pharyngitis, and therefore all cases of acute pharyngitis, especially in children, should be watched. It is very important, from a therapeutic standpoint, to recognise the cases in which the affection is due to rheumatism and gout.

Treatment.—In milder forms very simple treatment is generally sufficient, such as a hot mustard and water foot-bath and a Dover's powder at bedtime. A menthol spray (℞ Menthol ʒss. Ol. adepsin pur. ℥j.), sprayed several times a day by means of an oil atomiser, and sucking ice will greatly relieve the local inflammation. When the larynx and trachea are involved, the inhalation of tincture of benzoin, or a mustard poultice applied to the chest, is serviceable. The bowels should always be freely moved by saline aperients. For the rheumatic cases salicin, and for the gouty colchicum and alkalies are required. As the local inflammation subsides we may prescribe the compound krameria pastil, but local astringent applications are rarely necessary.

Chronic Pharyngitis.—The causes of chronic pharyngitis are many and diverse, and often enough they are remote and obscure. The characteristic objective conditions in the pharynx are commonly seen in very young children, while the subjective symptoms are generally observed from the age of eighteen onwards. In children the lymphoid tissues are especially active; and not only are the palatine and rhino-pharyngeal tonsils well developed, but the same excess is found in a much less degree in the smaller aggregations of lymphoid tissue around the muciparous glands. Thus, when from various causes a pathological condition of hypertrophy arises in the post-nasal and palatine lymphoid structures, constituting post-nasal adenoids and chronic enlargement of the tonsils, we very frequently observe a concomitant hypertrophy of the pharyngeal lymphoid tissue which, like the tonsils, participates in the tendency to atrophy in later life.

Thus in some cases the disease is congenital in origin; in others, catarrhal attacks, measles, or scarlatina leave behind them a similar hypertrophy, or increase that which may already be in existence. At puberty chlorosis and general anæmia, dyspepsia and constipation are fruitful causes of granular pharyngitis—the former two perhaps the most fruitful; later in life dyspepsia, gout, rheumatism, the irritation of tobacco smoke, alcoholic drinks, and so forth, operate in a like manner: but the pharyngitis in these cases is accompanied by general irritation and congestion of the whole pharyngeal mucous membrane; consequently, while on the one hand we may meet with enlarged lymphoid nodules only, as in granular pharyngitis, in these latter conditions there is also general thickening of the mucosa, with enlargement of the vessels and secretion of tenacious mucus in the rhino-pharynx and pharynx. If the patient suffered in childhood from post-nasal adenoids which have not completely atrophied, and if chronic nasal catarrh has persisted, there is a copious secretion of unhealthy sticky mucus in the rhino-pharynx, and the condition is known as post-nasal catarrh.

Thus it is impossible altogether to separate the simple catarrhal and chronic hypertrophic forms; they generally coexist, though the characteristics of the one or the other may predominate.

Many cases, especially those due to constipation and dyspepsia, or to portal congestion, are regarded by one of us (W. W.) as toxic in origin, and due to a failure on the part of the liver to arrest and destroy toxines resulting from imperfect digestion or decomposition in the intestinal tract; these toxines, like belladonna, have a specific effect on the pharyngeal mucous membrane. The soreness, stiffness and hyperæmia, the dryness of the throat and pain in deglutition, which are characteristic of belladonna or muscarin poisoning, are simulated very closely by the sore throat of dyspepsia following a late and heavy meal; and these conditions by frequent recurrence, even in a mild degree, eventually bring about permanent structural alterations of the mucous membrane. We may explain the occurrence of gouty pharyngitis in much the same way.

The pain often complained of is generally attributed to the implication of the nerve-endings in the degenerated granules; it is, however, more probable that the nerve filaments are irritated by the same causes which produce such very obvious hyperæmia and thickening of the mucous membrane; but the factor of temperament is clearly seen in the painful character of the chronic pharyngitis in chlorotic girls and in those of the neurotic temperament.

In later life the pharyngeal mucous membrane may become more or less atrophied, and the secretion of mucus very deficient—a condition sometimes distinguished by the term *atrophic pharyngitis* or *pharyngitis sicca.*

Thus it will be seen that chronic pharyngitis is generally due to several factors acting conjointly, which may be classified as follows:—

(i.) One of the most important is general anæmia. Granular pharyngitis is most frequently met with in anæmic girls, in whom also other signs of chlorosis exist.

(ii.) The strumous, rheumatic, and gouty diatheses. Gouty pharyngitis is usually characterised either by general or, more frequently, by lateral thickening, which often gives the appearance of thickened bands of tissue extending down the lateral walls of the pharynx behind the posterior palatine pillars.

(iii.) Dyspepsia and constipation, especially if associated with constipation or portal congestion, whether due to gastro-intestinal catarrh or heart disease, are prolific causes.

(iv.) Constant exposure to dust or irritating vapours, as in mattress-making, stone-dressing, tobacco-manufacturing.

(v.) Abuse of alcoholic drinks; it is also said to result from the use of irritating condiments.

(vi.) Recurrent acute attacks of catarrhal pharyngitis, or measles, scarlatina, and other exanthems.

(vii.) Improper methods of voice production, resulting in congestion of the mucous membrane of the fauces; and excessive use of the voice during an attack of acute or subacute pharyngitis.

Symptoms.—In making a diagnosis of chronic pharyngitis, it is very important to remember that every departure from the ideal normal pharynx does not constitute disease; that in fact nearly all the objective conditions observed in this affection may be present without producing symptoms, and in this disease there is no constant relation between the physical signs and the subjective symptoms. The patients are apt to complain of a constant irritating cough, and a sensation as of a hair or foreign body in the throat which they cannot get rid of; or of soreness and aching often amounting to sharp pain, especially in swallowing: often also there is a sense of weakness and discomfort in the fauces. The symptom for which advice is most usually sought, however, is impairment of vocal power. Hence professional and amateur singers, clergymen, public speakers, lawyers, and schoolmasters form by far the largest contingent of those who seek advice on account of chronic pharyngitis. Their complaints are various. Most frequently it is stated that the voice is readily tired and deficient in resonance and timbre; singers usually complain of deficiency or even of loss of the higher notes. These alterations in the voice are even more marked in those younger patients in whom post-nasal growths occupy the rhino-pharynx. Prolonged speaking, or singing, in the presence of marked chronic pharyngitis, often results in aching in the throat and back of the neck, whilst the voice gets weaker and weaker. After this has continued for a time the larynx becomes more or less congested, and then the voice, for public speaking, often goes altogether.

In patients who are suffering from simple catarrhal pharyngitis the chief features are the constant accumulation of mucus in the throat, the necessity for perpetual hawking, and the tendency to gagging and retching.

On examining the pharynx the mucous membrane is found to be diffusely congested. In the simple catarrhal forms it is bluish pink, with enlarged venules coursing over the posterior wall, which is often more or less covered by collections of mucus. The mucous membrane of the uvula and soft palate is sometimes considerably congested, thickened and granular, and some enlarged mucous glands are seen. The tonsils are often somewhat enlarged, with gaping crypts, and the larynx, especially the inter-arytænoid fold, is injected; some hypertrophied lymph follicles are always observable, in granular pharyngitis there is often little else to be seen. There is seldom any excessive accumulation of mucus; in fact the complaint very often is that the throat is too dry. In some cases, and particularly in the gouty, the lateral bands of hypertrophic tissue stand out prominently.

Treatment.—Before entering on the question of treatment it is desirable to lay stress on the necessity for attending to any primary dyscrasia, instead of relying solely on local treatment. Thus, in the great majority of cases, the general treatment of chronic pharyngitis is of far greater importance than the local. Anæmia and chlorosis must be combated with Blaud's pills and aperients; gout and rheumatism, constipation, dyspepsia, and portal congestion require each its appropriate treatment; while in other cases, as in many clergymen and schoolmasters suffering from granular pharyngitis, the health is more or less impaired and general nervine tonics are indicated; though, as a rule, the relief is unfortunately only temporary. Many patients will be greatly benefited by a course of alkaline or aperient waters, such as those of Aix-les-Bains, Ems, Mont Dore, La Bourboule; and, for gouty patients, Kissingen, Marienbad, or a gentle Carlsbad course is advisable.

Local treatment, however, is often required. The usual astringent lozenges, sprays, pigments, and gargles are most disappointing and inefficient. A very useful spray for general use in relaxed throat is a pinch of salt dissolved in a wineglassful of cold water. If the mucus tend to collect in the pharynx and rhino-pharynx, a solvent coarse spray, composed of bicarbonate of soda (1 to 2 per cent) with a few grains of boracic acid, may be used once or twice daily. A pastil containing 2 grs. of guaiac resin, ½ gr. powdered cubebs, $\frac{1}{20}$ gr. of emetine, and ¼ gr. of menthol, slowly dissolved in the mouth four or five times daily, will often relieve rheumatic forms of pharyngitis, while ¼ of a grain of codeine in the form of a pastil, and repeated if necessary, is useful in relieving the constant cough which in some cases of irritable pharyngitis interferes with sleep.

Enlarged granular lymphoid follicles should be destroyed by the galvano-cautery. Having previously cocainised the part (with a 10 per cent solution of cocaine), a small flat platinum or porcelain burner is placed on the centre of a granule when cold; the current is then turned on to a cherry red heat and immediately withdrawn. If there are any enlarged veins on the posterior pharyngeal wall they may be divided in places in a similar manner, so as to obliterate them; if left, they tend to maintain the vascular engorgement and general congestion. After using the galvano-cautery the patient should only take bland or cold food for a day or two; sucking ice may be grateful to him for a few hours after the operation, or a spray of cocaine (2 per cent dissolved in ol. adepsin pur.) may be used with an atomiser to relieve pain and soreness.

A pellicle forms on each cauterised spot, which separates in a day or two, leaving a clean surface. The cauterisation may be resumed, after an interval of three days to a week, till all the granules have been destroyed in turn.

Thickened bands of mucous membrane, when present, should likewise be destroyed by the galvano-cautery. If, as is sometimes the case in gouty pharyngitis, the lateral bands are very much thickened, they may be more quickly removed by the knife. Other methods of destroying the granules can only be recommended when the galvano-cautery is not available. The best alternative is to touch the centre of each with chromic acid fused on a silver probe, or curettement.

Great stress must be laid, of course, upon the future avoidance of those causes of irritation to which the malady was due; such as improper use of the voice, insufficient exercise, abuse of alcohol, or excessive smoking.

Hæmorrhage from the pharynx.—Hæmorrhage from the pharynx is deserving of special note, not so much on account of the actual causes of bleeding in this region, but of the frequency with which patients complain of "bleeding from the throat," and of the gravity of the pulmonary disease which is only too often the actual source of the loss of blood attributed to the throat.

Causes.—The chief causes of bleeding from the mouth and throat are—(*a*) Alterations in the condition of the blood in various pathological states, such as purpura, pernicious anæmia, leukæmia, mercurial stomatitis, hæmophilia, renal affections, and various acute fevers, especially typhoid fever and yellow fever. (*b*) Suppuration and ulceration, as in malignant disease, lupus, or syphilis. (*c*) The oozing of blood from spongy gums. (*f*) Post-nasal adenoids. (*g*) So-called vicarious hæmorrhage in women at the menstrual period. (*h*) Rupture of enlarged veins in the pharynx, especially in gout, and atrophic cirrhosis of the liver. (*i*) Laryngeal hæmorrhage in so-called hæmorrhagic laryngitis; in laryngitis sicca with bleeding after separation of crusts, traumatism, abrasions caused by swallowing hard angular bodies in food, surgical operations, and so on. (*e*) Epistaxis with escape of blood into the pharynx.

Yet with all these possible sources of hæmorrhage from mouth and throat, patients who seek advice for bleeding from the mouth generally are subjects of pulmonary hæmoptysis. Doubtless the mistake is owing in part to the very prevalent misconception that, unless the blood is coughed up or vomited with food, it cannot come from the lungs or stomach; while, on the other hand, bleeding from the gums or streaks of blood from a congested pharynx after violent coughing and hawking do not, as a rule, attract much attention: moreover, hæmorrhage from the throat from all other causes is either very rare or only secondary to graver general affections.

Symptoms.—A capillary oozing from the gums, or from any part of the pharynx, simply gives rise to a taste of blood, and is spat out mixed with saliva. If the oozing of blood occurs during sleep in the recumbent position, the blood may be hawked up with a small quantity of frothy mucus, and so give the impression that it is coughed up from the lungs. On examination, the real source of the hæmorrhage may be discovered; but very often this is impossible. If the bleeding be more copious, it may still be possible to examine every part of the upper respiratory and food passages for the bleeding point; but if the blood be poured out too rapidly for any such examination, the head should be held low, so that the blood can run out of the mouth. If it does so without coughing or retching, the source of hæmorrhage is almost certainly from the mouth, nose, or throat.

It is more difficult to determine the source of hæmorrhage when a patient, without any signs of lung disease, states that a tickling sensation arises in the larynx, and on coughing slightly blood comes in considerable quantity. Of course, if there be evidence of pulmonary disease, or if the blood when coughed up is frothy and bright red, there can be little doubt that it has come from the lungs; but blood which has come from the throat may be bright red, frothy, and mixed with saliva, and on the other hand a pulmonary hæmorrhage may be unmixed with air. One point of distinction lies in the fact that in pulmonary hæmorrhage the blood continues to be coughed up with frothy mucus for an hour or two, and that the expectoration generally shows evidence of altered hæmoglobin for some days; whereas when blood comes from the mouth or larynx it is soon got rid of completely by coughing and spitting, and, if none is poured out subsequently, all trace of the hæmorrhage will disappear in an hour or two. Still, with all these differential signs, it is sometimes extremely difficult to make out the true source of the hæmorrhage with certainty.

It is important to remember that tuberculous disease of the lungs often manifests itself by hæmoptysis, and that the initial hæmorrhage may be considerable without the presence of any physical signs. If, therefore, a patient present himself with a statement that he has had a hæmorrhage from the throat, if the pulse rate is persistently increased in frequency, and especially if the temperature is raised at night, then, even though there may be no other evidence of tuberculous disease of the lung, and even if no tubercle bacilli be detected in the expectoration, he should be treated as though the hæmorrhage were pulmonary; unless of course there be direct evidence that the blood actually came from the throat.

Treatment.—The treatment must be guided by the cause of the hæmorrhage. If it be due to injury, the patient may suck ice, and sprays or local applications of some astringent solution, such as tannic or gallic acid, catechu, matico, or calcium chloride, may be employed; or if the bleeding point can be seen it may be touched with the galvano-caustic point. It is sometimes possible to secure and twist the ruptured vessel with torsion forceps. These simple methods, together with the other general measures which are usually adopted in hæmorrhage, generally suffice to check bleeding from the rupture of small vessels in the mucous membrane of the pharynx or larynx from all causes, if indeed it do not cease spontaneously; but it has sometimes been necessary to ligature the common carotid artery on account of the hæmorrhage arising from a suppurating tonsillitis or a malignant growth.

The bleeding having been checked, attention should be directed to the treatment of the underlying cause of the hæmorrhage, whether it be a local condition of the throat, or disease of the liver, heart, or kidneys, or a general systemic affection.

Diseases of the uvula.—The uvula being practically a part of the soft palate, it is very frequently implicated in diseases affecting that region, while its affections present some special features.

Congenital absence of the uvula occurs especially in association with cleft palate; or the uvula may be more or less completely bifid, representing an incomplete cleft palate.

Inflammatory affections.—In acute inflammatory diseases of the pharynx, from whatever cause, the uvula generally becomes inflamed; and in septic inflammations it is especially liable to become so enormously swollen and elongated that it may even approach the size of the little finger. Sometimes it is long enough to be grasped between the teeth when coughed forward to the front of the mouth, or to fall into the larynx when drawn backwards and downwards.

An œdematous uvula may be freely scarified, and, when the inflammation is acute, sucking of ice may be grateful to the patient. In other respects the treatment does not differ from that of the pharyngeal affection with which it is associated.

Chronic uvulitis is usually associated with chronic pharyngitis, the velum palati and uvula being relaxed and congested, and the latter frequently elongated; while enlarged venules and mucous glands are found scattered over the surface.

Elongated uvula.—An exaggerated importance is only too frequently attached to the uvula as a source of many and various symptoms in the region of the throat; we must therefore express at once our decided opinion that it is in very rare cases only that the condition of the uvula can properly be regarded as the cause of any notable symptoms; in the vast majority of patients whose symptoms are attributed to the uvula, these are really due to morbid conditions in other parts of the upper respiratory tract.

We may conveniently classify cases of elongated uvula into two subdivisions, viz. (*a*) those in which the uvula is merely relaxed, the mucous membrane extending some distance below the muscular structures but without congestion or hypertrophy; and (*b*) those in which hypertrophy and chronic congestion are present, often associated with degeneration of the glandular structures of the naso-pharyngeal mucous membrane.

Symptoms.—In a great many cases, unless the elongation be very marked indeed, there are no symptoms whatever. In the milder cases, where there is merely relaxation of the soft palate and uvula without hypertrophy or congestion, the symptoms complained of are mainly impairment of the quality and strength of the voice, and are mostly observed in professional singers. But the alteration and impairment of voice are often due rather to the relaxation of the soft palate, interfering with the proper movements of the uvula in singing high notes, than to the elongation of the uvula in itself. In well-marked cases patients usually complain of continual hawking, with a sense of some foreign body in the throat. The cough is sometimes very severe and persistent, particularly on lying down at night. The constant titillation at the back of the tongue not infrequently results in vomiting; this is especially in the morning or after meals, and, if the elongation be so considerable that the uvula reaches down to the larynx, laryngeal spasms may occur. In men much addicted to abuse of tobacco and alcohol the last-named symptoms are particularly frequent. In a few and very rare cases the constant pain and irritation in the throat, persistent cough and frequent vomiting, may result in emaciation and weakness; while the recurrent hæmorrhage from rupture of enlarged vessels in the pharynx may, in conjunction with the other symptoms, give rise to the suspicion of serious lung mischief.

Treatment.—When really necessary, and when all other sources of the symptoms presented have been excluded, ablation of the uvula should be performed; but here again we would emphatically state that in our opinion the operation is very rarely necessary.

The cases in which uvulotomy are required are—(i.) In professional singers suffering from loss of vocal tone without appreciable affection of the larynx, and in whom the uvula is elongated, thickened, and relaxed; (ii.) in cases where the elongation is so considerable that it becomes sucked into the larynx and produces attacks of suffocation, especially during sleep; (iii.) when a long and thickened uvula is associated with a persistent tickling cough, and when, after careful examination of the pharynx and larynx, all other possible causes for the symptoms have been excluded; (iv.) in malignant disease of the uvula; (v.) and, finally, in cases where a much elongated uvula is an obstacle to the performance of delicate intra-laryngeal operations. When cases are properly and judiciously selected the result is most gratifying, sometimes altogether out of proportion to the relatively trivial operation. The great amount of benefit that may be derived from such a simple procedure as removal of the uvula was well illustrated in a case observed by one of us (W. W.). The patient presented the wan and wasted appearance of advanced consumption, and had in fact been treated for pulmonary tuberculosis. He was certainly very feeble and emaciated, and crepitation could be heard over both lungs. After his uvula was partly removed the improvement and final recovery were rapid; three pounds in weight were gained during the first fortnight.

In performing uvulotomy, the parts having been well cocainised, the tip of the uvula—unless the uvulotome be used—should be seized with forceps and gently drawn forward. The redundant portion is then removed by one cut with a pair of curved blunt-pointed scissors. By operating in this manner the cut surface comes to be posterior, and irritation by food on deglutition is avoided.

The whole uvula should not be removed, but the redundant part only. If too much has been taken away, patients often complain of "want of power" in the throat, and sometimes of difficulty in speaking or reading aloud.

For a few days after the operation the patient should avoid talking, and the food should be soft, bland and cold. A spray may be used containing cocaine and phenazonum dissolved in glycerine and water; or a mild morphine and cocaine pastil should be sucked at intervals, especially before meals. The pain and irritation resulting from the operation are generally considerable, and last from two to five days, being altogether disproportionate to the smallness of the cut surface. Secondary hæmorrhage may occur two or three days after the operation, hence the importance of the patient avoiding all hard or even solid food.

Chronic infective diseases.—Syphilis or tuberculosis, for instance, may attack the uvula, the symptoms and treatment being the same as in these diseases when affecting the fauces.

Growths of the uvula comprise papilloma, mucous polypus, and carcinoma. [See "New Growths of the Pharynx," p. 752.]

Paralysis of the uvula occurs in association with paralysis of the velum palati. Paralysis of the uvula alone may occur as a consequence of diphtheria.—F. S. and W. W.

The throat affections of the specific febrile diseases.—These affections will be described under the heads of the respective diseases, but it has been thought well to make some reference to them in this place.

Small-pox.—A certain amount of catarrh of the pharynx and larynx is met with in most cases of small-pox. In some cases pocks are seen on the pharyngeal and laryngeal mucous membrane, but, owing to the presence of moisture, well-marked pustules are seldom seen. The pustules give rise to the symptoms of laryngitis about the sixth day; but it is not until the ninth to the twelfth day that grave symptoms, due to an œdematous condition of the larynx or to the formation of a false membrane, occur. With either of these complications the disease may run a rapid and fatal course; occasionally deep ulceration followed by necrosis of the cartilages occurs; if not immediately fatal, the resulting cicatrisation and contraction lead to stenosis of the larynx. In the malignant form of small-pox hæmorrhagic extravasations may be seen in the laryngeal mucous membrane.

Treatment.—If the eruption is limited to the mouth and pharynx antiseptic or slightly astringent gargles may be employed The laryngeal complications must be treated after the manner described for idiopathic affections of the larynx.

Varicella.—The vesicles of chicken-pox have been noticed in the mouth.

Measles.—Preceding the cutaneous rash is seen an eruption of small red points or patches on the roof of the mouth and palate, to which the term endanthem has been applied. Pharyngeal and laryngeal catarrh is an invariable accompaniment of measles. In young children a certain amount of spasm is present, which gives rise to croupy attacks. In severe cases the inflammation may go on to ulceration and even to the formation of an abscess. Membranous laryngitis is a rare but very dangerous complication of measles.

The treatment of the laryngeal affections of measles differs in no respect from the treatment of similar affections due to other causes.

Rötheln (German measles).—There is almost invariably a certain amount of soreness of the throat, and the soft palate and fauces will be found injected and swollen.

Scarlet fever.—For a full account of the throat affection of scarlet fever the reader is referred to the article on the disease (vol. ii. p. 122). In this place it will only be necessary to refer to the formation of a false membrane over the palate and fauces, which sometimes accompanies the sore throat of scarlet fever. The exudation which is often seen on the fauces during the acute stage of scarlet fever is not caused by the Löffler bacillus, and is therefore not true diphtheria. It is possible, however, that diphtheria may accompany the acute stage of scarlet fever, but this is very uncommon. On the other hand, the membranous exudation occurring on the fauces during the convalescent stage of scarlet fever, being caused by the diphtheria bacillus, is true diphtheria. Post-scarlatinal diphtheria usually occurs at a late period of convalescence.

Influenza.—A catarrhal condition of the pharynx and larynx exists in almost all cases of influenza. Implication of the pharyngeal tonsil is not at all uncommon, and follicular inflammation occasionally occurs.

Acute pharyngeal catarrh and follicular tonsillitis with or without peritonsillar inflammation are frequently seen. In the larynx all conditions of inflammation are met with, from slight catarrh up to œdema or the formation of an abscess. The expectoration is occasionally tinged with blood, and cases of hæmorrhagic laryngitis have been seen as a result of influenza. Superficial ulceration of the vocal cords not infrequently occurs. A notable feature of influenzal laryngitis is the protracted course which it runs. Laryngeal paralysis is a not infrequent sequel of the disease.

Enteric fever.—Erythema of the pharynx may occur at the commencement of enteric fever, but it presents no characteristic features. In some severe cases of enteric fever a few small shallow ulcers, not larger than a linseed, have been noticed on the soft palate. Their borders are well defined and have an inflammatory zone, and the surface of the ulcers is covered with a grayish film. The ulcers are not painful, there is no glandular enlargement, and typhoid bacilli are not present in them.

A secondary diphtheritic deposit may occur on the fauces of patients with enteric fever; this is a grave complication.

The most important of the throat affections of enteric fever is laryngitis, which may occur at the very beginning of the attack, or be one of its later manifestations. Bacteriological investigation confirms the clinical view that these laryngeal affections are directly due to localisation of the typhoid virus and are not complications.[1] The presence of the bacilli of typhoid prepares the ground for the settlement of other micro-organisms, including the pus exciters; and these are responsible for the secondary processes which are sometimes observed.

In those cases in which laryngitis occurs at the outset the symptoms of the local malady may so completely obscure the general condition that it is not until the appearance of an eruption, and of abdominal symptoms, that a definite diagnosis can be made. Usually, however, the symptoms of laryngitis show themselves in the third week, and the local disease runs an acute course; ulceration may occur, and this may be the first stage of the severe affection to which the term of "laryngo-typhus" has been applied by German writers. Hoarseness, dyspnœa (chiefly affecting inspiration), difficulty and pain in swallowing, are generally present. Tracheotomy is frequently necessary on account of œdema of the larynx or purulent infiltration of the mucosa. The occurrence of these acute cases of laryngitis, with ulceration and the presence of the Eberth-Gaffky bacilli in the part, points to the possibility of enteric fever being communicated by the breath and expectoration. In some cases the laryngeal affection is not recognised until convalescence has begun, or even after complete recovery. In such cases the signs of stenosis of the larynx are the most characteristic; and death may occur from œdema of the larynx or impaction of a piece of necrosed cartilage in the glottis. On account of the extensive ulceration and necrosis which occur, tracheotomy is often required; and if recovery take place, it is seldom possible to dispense with the canula on account of collapse of the larynx and cicatricial contraction.

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[1] According to Kanthack and Drysdale, these laryngeal ulcers are usually due to pyogenetic organisms and not to the typhoid bacillus.

It is not uncommon to find an affection of the larynx on post-mortem examination, although during life there were no symptoms indicative of any laryngeal trouble.

Typhus fever.—Changes similar to those seen in enteric fever are also met with in typhus.

Whooping-cough.—In this disease there is slight catarrh of the larynx in the first stage, which becomes intense during the spasmodic stage; and the hyperæmia extends into the trachea.—F. DE H. H.

Acute septic inflammations of the pharynx and larynx (including phlegmon of the cellular tissue of the neck—Angina Ludovici).—Under this heading we include a number of forms of acute septic inflammations of the pharynx and larynx which hitherto have been usually considered as pathologically different; such as acute inflammatory œdema of the pharynx and larynx, phlegmon of the pharynx and larynx, and erysipelas of these parts. In our opinion phlegmonous cellulitis of the neck (angina Ludovici) also comes under this head.

In a recent communication to the Royal Medico-Chirurgical Society,[1] one of us (F. S.) argued, on clinical and bacteriological evidence, that these various forms of acute septic inflammation of the throat should be considered as varying degrees of virulence of one and the same pathological process. The primary seat and subsequent development depend in all probability upon accidental breaches of the protecting surface through which the pathogenetic micro-organism, which causes the subsequent events, finds an entrance; and it is absolutely impossible to draw any definite line of demarcation between the purely local and the more complicated cases, or between the œdematous and the suppurative forms. That each and all of these septic processes may be produced by several pathogenetic organisms does not, in our opinion, in the least speak against their pathological identity. These micro-organisms are "interchangeable" in the sense that each and all of them, when penetrating into the tissues, produce one and the same effect; namely, an acute septic inflammation—œdematous, purulent, or gangrenous. Likewise we believe that erysipelas etiologically considered is not a specific disease; usually it is caused by the streptococcus pyogenes, but it may also be produced by the staphylococcus pyogenes aureus, as Max Jordan's researches have definitely proved. The micro-organisms causing erysipelas most probably enter into the circulation in every case; pyæmia following erysipelas is therefore primary, and not due to a mixed infection.

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[1] We must refer readers interested in this subject to this paper (*Trans. Roy. Med.-Chir. Soc.*, vol. lxxviii. p. 161) and to its discussion (*Proc. Roy. Med.-Chir. Soc.* 3rd series, vol. vii.) for the particulars which considerations of space will not allow us to discuss at length in this chapter.

When we attempt to draw definite distinctions between the inflammations associated with different micro-organisms we fall inevitably into a confusion of terms. In the discussion on Semon's paper Dr. Kanthack gave most valuable support to our views by quoting in detail four cases of his own in which various pyogenetic micro-organisms had been found producing various stages of the same process. Thus these cases bacteriologically distinct were pathologically identical (see also vol. i. pp. 533, 536).

Etiology.—The affections here discussed are due to the invasion of the system by pathogenetic organisms, of which, so far, the streptococcus pyogenes appears to be the most frequent. No doubt, however, any one of the other pyogenetic microbes, such as the staphylococcus aureus or citreus, the micrococcus tenuis, the bacillus coli communis, the bacillus pyocyaneus, and so on, if by chance it multiply sufficiently, may alone produce an acute septic inflammation indistinguishable, except from a bacteriological point of view, from the streptococcous inflammation.

Pathology.—Pathologically these inflammations are characterised by a violent exudation into the tissues affected. This exudation may be serous, sero-purulent, purulent, and in the worst cases may even lead to gangrene. All these various forms, however, merely represent various degrees of intensity of inflammation, not differences in kind.

Symptoms.—For clinical purposes we may recognise four degrees of inflammation:—(*a*) Superficial septic inflammation, as in the so-called "hospital sore throat"; (*b*) Œdematous inflammation, as acute œdematous tonsillitis, uvulitis, pharyngitis, epiglottiditis, arytænoiditis, cellulitis of the tissues of the neck, and so forth; (*c*) Suppurative inflammation or phlegmon; (*d*) Gangrenous inflammation.

Septic inflammations of the throat attack persons of all ages and both sexes, very frequently even those apparently in perfect health; though in those who are run down in health from any cause, or are suffering from some debilitating affection such as diabetes, the disease is especially prone to occur and to run a severe course.

We know nothing definitely about the length or even the existence of an incubation stage. Prodromal symptoms, such as headache, feverishness, sore throat, and general malaise, may precede the onset of more acute symptoms for a few days. In the slighter forms, as in hospital sore throat, there may be only localised soreness and stiffness in the throat, with headache and general malaise, without fever or marked constitutional disturbance. These mild cases, however, may pass into the more severe forms. In the grave forms often enough the disease manifests itself quite abruptly. It may be ushered in by a rigor and rapid rise of temperature. The course of the fever is very variable, as it probably depends on the virulence of the septic infection in the individual case; and, while usually ranging high, it may never rise above 100° F., especially in asthenic cases; or it may present a remittent or relapsing type: but the temperature as a rule reaches its highest point at the very onset. Rigors occurring later in the course of the disease generally indicate further complications or the onset of suppuration. The urine is febrile; the frequency of albuminuria has yet to be determined; sugar is found comparatively often. The pulse during the acute stage is usually frequent, full, and bounding, but soon becomes weak and compressible. When suppuration has occurred and the strength is greatly reduced, the pulse is small and thready, and perspiration profuse.

In those rare cases in which the nervous centres are involved early, the pulse and respiration become irregular, and the patients are generally delirious by the second or third day.

Whether the part attacked be the fauces, pharynx, larynx, or cellular tissue of the neck, the first symptom usually complained of is sudden pain in the throat and difficulty in swallowing, which within a few hours may amount to complete aphagia. If the larynx be involved, hoarseness of voice and, soon after, laryngeal stridor are observed. Often the aphonia is complete. The aphagia and dyspnœa last for a few hours to a few days; but in the cases of recovery, these and all other symptoms rapidly subside.

Objectively the symptoms vary, of course, with the seat of the inflammatory process. In the great majority of cases the pharynx is first affected, and more especially the tonsils—the latter, with their anatomical configuration, forming a natural portal for the entry of infecting micro-organisms into the body. This process was fully considered in F. Semon's paper, to which we have referred. On the other hand, the microbes may pass on farther to find a point of invasion in the tissues lower down, in the larynx—and here especially in the epiglottis, or in the cellular tissue of the neck.

When the tonsils are primarily affected, the inflammation—clinically speaking—hardly differs from ordinary acute follicular tonsillitis. In the case of the pharynx rapid œdematous swelling occurs, and the uvula may be greatly elongated and thickened to the size of the little finger. The swelling is often distinguished by a peculiar bluish discoloration. After a few days, if suppuration do not occur, the swelling subsides, leaving the mucous membrane more or less wrinkled in appearance; or the inflammation may spread down to the larynx.

Some of the worst and most fatal cases begin in the pharynx and suppurate in the course of a few days, the septic inflammation remaining limited to that part (Senator's acute infectious phlegmon of the pharynx). More frequently it extends to the regions around, or spreads downwards, much more rarely upwards, to the naso-pharynx, the nasal passages, and even to the membranes of the brain. In the great majority of cases of septic pharyngitis the inflammatory process leaves this part in a few hours or days and extends downwards to the larynx. Here it appears that the epiglottis is generally most markedly affected, becoming enormously swollen and turban-shaped, so that by simply depressing the tongue it may often be seen as a semi-transparent scarlet or bluish-red roll. Next in point of frequency the arytænoids and the arytæno-epiglottidean folds suffer, and lose their characteristic shape in the enormous red or purple swelling which takes place; a swelling very often so great as completely to hide the ventricular bands and vocal cords. In such cases, as already mentioned, the voice at first is weak and hoarse ; in a day or two, or even in a few hours, complete aphonia and dyspnœa supervene, and the glottic chink is often so narrowed that at any moment there is great risk of an asphyxia so acute as to require the immediate performance of tracheotomy. In other cases the submaxillary or cervical cellular tissues become primarily infected, the pathogenetic micro-organisms gaining entrance from the mouth by a carious tooth or fissure in the mucous membrane, by the tonsil or pharynx, and causing a hard swelling under the tongue and a localised hard, brawny infiltration beneath the jaw—hitherto commonly named angina Ludovici—but in its eventual course spreading to the pharynx or larynx, or to other regions of the neck, and ending in resolution, or more usually in suppuration; whilst in the worst cases gangrene may ensue. In some cases diffuse purulent infiltration is met with, or abscesses arise in the œdematous cellular tissue or between the muscles of the neck. In the very worst cases metastatic abscesses occur either in the superficial parts or in joints. Except in its primary seat it is in onset, course, and event precisely similar to the disease as seen in the pharynx or larynx.

Whilst the purulent variety of the septic inflammation usually leads to speedy death, cases of serous inflammation of the larynx and its neighbourhood may get well within a few days, however considerable the inflammation. Here, again, it is characteristic that the maximum inflammation is usually attained within a few hours from its very onset; and that in the cases in which recovery takes place even considerable diminution of the swelling is the rule within a day or two from the beginning.

Often, however, the disease is not confined to the neck, but spreads, sometimes with incredible rapidity, to other parts. In addition to the lungs, in which patchy or general pneumonia may appear, the serous membranes are particularly liable to suffer ; and pleurisy (single or double), pericarditis, peritonitis, or meningitis may appear within a few days or even hours from the initial rigor. As in the original seat of the disease, the exudation of the serous membranes may be either of a serous or of a purulent character; sometimes it is fibrinous. Even in cases complicated with pneumonia, pericarditis, and pleurisy, recovery is possible; and if it does occur, is remarkable for its quickness and completeness. In more severe cases, however, death ensues with signs of increasing coma and heart failure; and in the worst of them the whole process from beginning to end may not occupy more than ten to twelve hours.

In very rare cases it appears as if the whole brunt of the septic infection, apart from the parts first attacked, fell upon the central nervous system. In such cases epileptiform convulsions, delirium, irregularity of the heart and pulse, are amongst the earliest symptoms; and death may occur with signs of severe septic infection of the nervous system, without any complications in the chest, and after the local inflammation of the pharynx and larynx has completely subsided.

Diagnosis.—Unless the patient be suffering from facial erysipelas the earlier symptoms and physical signs may give little indication of the grave nature of the disease, and it may easily be mistaken for acute tonsillitis or pharyngitis; but the rapidly progressing constitutional disturbance, the early onset of delirium, and especially the supervention of œdema of the larynx, should serve to put us on our guard. Early implication of the lymphatic vessels, and brawny induration of the neck, taken in conjunction with the other manifestations of a grave affection, should leave no manner of doubt that the case is one of septic inflammation. The bacteriological examination of the affected parts will reveal the species of microbe which in the individual case has caused the disease.

Treatment.—The necessity for prompt and energetic treatment in all forms of septic inflammation is but too obvious. Our aim must be directed towards controlling the local inflammation, to support the patient with light nourishment, and to watch for any symptoms of heart failure. Ice should be administered internally, and also externally by means of Leiter's tubes, or the ice-bag applied to the front of the neck. If there be œdema of the larynx, careful watch must be kept lest at any moment intubation or tracheotomy become necessary; and on no account should the patient be left if dyspnœa have arisen: in fact dyspnœa, if at all marked, is an indication for immediate intubation or tracheotomy, unless the laryngeal obstruction can be relieved by freely scarifying the parts affected.

Four or five grains of quinine should be ordered every four hours; and if the pulse be weak and there be any indication of heart failure, this may be combined with the tincture of perchloride of iron and digitalis. In such cases, or where pneumonia has supervened, one of us (F. S.) has found frequent inhalation of oxygen very useful. Light nourishing food must be given, and probably alcohol in the form of brandy or whisky. In suppuration, particularly in cases of phlegmonous cellulitis of the neck, the affected tissues should be incised, and the resulting wound treated antiseptically.

Retropharyngeal abscess.—*Causes.*—Retropharyngeal abscess is a—usually circumscribed—suppuration occurring in the tissues between the mucous membrane of the posterior wall of the pharynx and the spine; it is mainly a disease of early childhood, though occasionally it may occur in an adult.

The vast majority of cases must be called idiopathic, and due to inflammation of the lymphoid tissue of the pharynx arising, from no definitely assignable cause, in young children up to the age of four. The strumous diathesis and rickets dispose to its occurrence; or it may follow measles, scarlet fever, or injury. It is sometimes due to caries of the cervical vertebræ, or, in rare cases, to burrowing of pus from other regions; it is probable that not a few cases are septic in origin, especially in older patients. The affection may follow injury from blows or foreign bodies. One of us (F. S.) has twice seen it occur in association with adenoid vegetations.

Pathology.—In children there is an aggregation of lymphoid tissue in the posterior wall of the pharynx opposite the second and third cervical vertebræ; and the suppuration is usually due to inflammation and breaking down in this tissue on one or other side: the abscess is rarely central. In adult patients the suppuration occurs in the cellular tissue which remains after the involution of the lymphatic tissues of the pharynx. The abscess is generally confined to the oro-pharyngeal region, and, though it may burrow down towards the œsophagus, it very rarely extends upwards much above the level of the soft palate.

The glands below and behind the angle of the lower jaw on the side of the abscess usually become enlarged, indurated and inflamed.

The abscess may rupture spontaneously into the pharynx, or burrow in various directions; the inflammation very often extending to the larynx with resulting acute laryngitis or œdema.

Symptoms.—The onset may be acute or chronic. If acute, there is general pyrexia, sometimes preceded by a rigor with local heat and painful tumefaction which, on inspection or digital exploration, is seen as a fluctuating bulging of the posterior pharyngeal wall. As a rule, the voice is husky or aphonic; and cough resembling croup is usually present, accompanied by more or less acute dyspnœa. The child's cry has a peculiar throaty tone. Fixation of the head is usually a marked feature. In the more chronic cases the symptoms are much the same, but the temperature is not raised. In adults difficulty and pain in deglutition are the chief subjective symptoms. In children it is more difficult to detect the bulging abscess.

Diagnosis.—The symptoms in young children are easily mistaken for croupous laryngitis; but in retropharyngeal abscess deglutition as well as respiration is difficult: moreover, the fixation of the head and the unilateral swelling below the jaw point to retropharyngeal abscess. The chronic form has to be distinguished from sarcoma, which grows rapidly, does not fluctuate, often has an irregular or nodular surface, and is rarely attended by actual rigidity of the head.

The prognosis in very young children should be guarded, especially when the symptoms of laryngitis are decided; in older children and in adults the prognosis, under appropriate treatment, is always favourable. Untreated, the rupture of the abscess in the pharynx is liable to cause suffocation from the pus entering the larynx; while the danger of œdema of the larynx causing acute asphyxia is very considerable. Needless to say that any underlying affection, such as caries of the cervical vertebræ, would greatly modify the prognosis as regards complete recovery.

In the acute cases of adults there is even more need for a cautious prognosis, as they sometimes take the peculiarly fatal course and character of acute septic pharyngitis—the so-called acute infectious phlegmon of Senator.

Treatment.—In all acute cases young children should be placed in a steam bed, while adults should frequently use medicated steam inhalations. The treatment consists in evacuating the pus as soon as fluctuation is detected, either through the mouth by the knife, or, especially if the case is complicated by cervical caries, by an incision behind the sterno-mastoid muscle under strict antiseptic precautions. The operation through the mouth should always be done with the patient's head hanging low down, to avoid the danger of pus escaping into the larynx. Of course if the pus be actually pointing behind the sterno-mastoid, or elsewhere, this will determine the seat of evacuation. Aspiration is often recommended, but refilling of the abscess cavity is more likely to occur.

The great danger lies in the occurrence of œdema of the glottis. Ice should be sucked if the patient be old enough, and hot applications made to the neck and submaxillary region. Young children should be kept in the steam bed, and any symptoms of obstructive dyspnœa carefully watched for; as intubation or tracheotomy may at any moment be urgently required, even for some little time after the evacuation of the abscess.

Pharyngomycosis leptothricia.—The leptothrix fungus and spores are almost invariably present in the concretions of tartar that gather round the teeth, and on the papillæ of a coated tongue; and very frequently they may be found in the crypts of the tonsils. Under certain conditions they take root in the tissue and germinate, forming characteristic milky-white chalk-like out-growths. The fungus grows from the bottom of the crypts and acinous glands, and is most frequently seen on the palatine and lingual tonsils; though the soft palate and uvula and posterior pharyngeal wall also are often the seat of the growth. Under the microscope the elongated cylindrical or thread-like cells of the cryptogam will be found, together with a certain amount of amorphous granular matter. The mucous membrane around the growths of fungus is healthy, but the masses are remarkably adherent and often cannot be torn away without some of the epithelium of the matrix; though sometimes they are soft and break off short when removal is attempted.

The affection generally occurs in patients who are run down in health from one cause or another, and is especially apt to follow digestive disorders.

The symptoms are generally very slight or altogether absent, and often enough the patches are accidentally discovered by the patients. A certain degree of discomfort, stiffness, and dryness may occasionally be felt in the throat; whilst in some cases there is an irritating cough, and the voice may be impaired. It is very doubtful, however, how much even of these slight symptoms is directly due to the growths, and how much to the dyspeptic troubles and impaired health with which the affection is generally associated.

The only affection that may be confused with this mycosis is chronic lacunar tonsillitis with yellow caseous exudation in the crypts. The yellow masses, however, are readily extruded; whereas the leptothrix masses are very adherent and are chalk-white in colour. The leptothrix spores have been found in the cheesy masses of follicular tonsillitis; but it is only when they have taken root in the tissues that they constitute a real mycosis.

The absence of pain, febrile temperature, and constitutional disturbance at once distinguish the affection from acute tonsillitis or diphtheria.

The treatment should be directed to improvement of the general health. Many forms of local treatment have been advocated, but even when most vigorously and perseveringly carried out they are all very tedious, and fail to prevent the return of the fungus; whereas we have often found that with improved health the growth disappears spontaneously. Thus, in our opinion, in most cases at any rate, no local treatment is required.

Calcareous concretions in the tonsils are originated by the leptothrix buccalis in the tonsillar crypts, just as tartar is deposited on the neglected teeth; and around this nucleus altered mucus, pus, and epithelium cells collect and become calcareous. In this manner several such accumulations of calcareous matter may come to occupy the crypts; or one or more large calculi, varying in size up to more than an inch in diameter, may be formed. The symptoms are often very slight, and are simply those common to enlarged tonsils: sometimes they maintain a certain degree of chronic inflammation.

The diagnosis may be made by means of a probe or, in the case of larger deposits, by palpation.

The calculus should be removed, and if the tonsil be hypertrophied, or multiple small concretions be present, it is better to remove the gland at the same time.

Diseases of the lingual tonsil.—The fourth tonsil situated at the base of the dorsum of the tongue is liable to the same diseases as the palatine tonsils. Thus it may be the seat of acute lacunar or parenchymatous inflammation, which may suppurate. Treatment is the same as in acute tonsillitis.

Chronic hypertrophy is frequently found in a mild degree in chronic pharyngitis, and more marked—often without adequate explanation—in otherwise healthy persons, particularly in women. In the last-named class of cases, by direct contact of the hypertrophic glandular tissue with the dorsum of the epiglottis, it often gives rise to a constant irritating cough, sensations of fulness, choking, "lump in the throat," and so forth. Many cases of so-called "globus" are of this kind. The hypertrophied tissue is sometimes seen quite to overlap the epiglottis, often, indeed, almost to conceal it.

The hypertrophy should be reduced by applications of Lugol's solution (iodine grs. xx., iodide of potassium grs. xxx., to an ounce of water); or by the lingual tonsillotome, curette, or snare according to the shape and size of the mass. The employment of the galvano-cautery, which is often recommended, is not free from the risk of causing violent parotitis.

Tuberculosis of the pharynx.—*Etiology.*—The immediate and remote causes of tuberculous disease of the fauces and pharynx are the same as in pulmonary tuberculous disease, to which the pharyngeal affection, which is one of the rarer manifestations of tuberculosis, is almost invariably secondary. Occasionally the pharyngeal affection appears to precede or to appear simultaneously with pulmonary tuberculosis; but if we except the tonsils, primary pharyngeal tuberculosis is very rare. Chronic enlargement of the faucial or pharyngeal tonsils disposes these structures to tuberculous infection; but no definite reason can be assigned for the occurrence of the disease in the soft palate.

Pathology.—Pharyngeal tuberculosis may be either acute or chronic. Only two or three cases are recorded where the acute form was believed to be primary; the chronic variety is more frequently unaccompanied by evidence of pulmonary infection. The route by which the bacilli gain access to the infected tissues is not at present known. The old view that the pharyngeal tissue is directly infected by the sputum does not account for the fact that the deeper tissues are affected first; and that the superficial ulceration arises by the extension and breaking down of deeper-lying miliary tubercles. On the other hand, the tendency for tuberculous disease in this region to attack either the anterior surface of the soft palate, the posterior pharyngeal wall, or the laryngo-pharynx opposite the cricoid ring, suggests that slight or superficial abrasions produced in swallowing food provide the portal for the entrance of infection, which in the case of the tonsils is always present in the crypts.

The tonsils are much more frequently affected than hitherto believed; and we are of opinion that these glands are in many cases to be held responsible for the entrance of tubercle bacilli, as indeed of other microbes also into the system. Krueckmann has shown that tuberculosis of the cervical lymphatic glands almost always depends upon the invasion of the glands by way of the tonsils; and in no less than 60 per cent of cases of tuberculosis of the lungs examined on the post-mortem table by this observer, tubercles were detected in the tonsils: similar results had previously been obtained by Strassmann and Dmochowski. Many cases of pharyngeal adenoids have been proved to be tuberculous; in some giant cells have been demonstrated, while a very large proportion contain tubercle bacilli. Masked tuberculous disease of the tonsils undoubtedly occurs in the course of pulmonary tuberculosis; but it is probable that a similar condition of the tonsils often precedes the establishment of the lung affection.

The subsequent course of the tuberculous deposit differs in no respect from tuberculous disease in other regions; caseation and breaking down soon result in characteristic ulceration.

The symptoms of tuberculosis of the pharyngeal mucous membrane and of the tonsils differ in several respects; though many of the symptoms are common to all tuberculous processes.

The acute form of the pharyngeal affection usually begins with pain in the faucial region, which on examination is found to be hyperæmic and slightly swollen. The soft palate, if the seat of deposit, becomes stiff and paretic; and in the course of a day or two several discrete, muddy-gray miliary tubercles are visible, slightly elevated, but obviously below the translucent mucous membrane. The initial hyperæmia gives place to a more or less general anæmia of the soft palate, as the tubercles increase in number and coalesce. Very soon discrete or confluent ulceration of the tubercle occurs, and by superficial extension the originally small solitary ulcers coalesce and form a larger superficial ulcer covered with grayish white, diffluent, breaking down, caseating matter, and with irregular "worm-eaten" or "mouse-nibbled" margins which are flush with the surrounding mucous membrane. Fresh tubercles meanwhile appear, only to pass through similarly rapid phases of development.

Ere this the infiltration of the soft palate has resulted in failure of its functions; consequently the voice is nasal, and fluids escape by the nose on drinking. Deglutition becomes very painful, and coughing almost impossible; consequently the patient is unable to get rid of the copious, sticky, stringy, muco-purulent discharges covering the parts, which accumulate and dribble from the open mouth, or are expelled by feeble attempts at hawking. As in acute miliary tuberculosis of the lungs, the temperature ranges high, without presenting the hectic character; but the emaciation and general prostration are more rapid.

In the more common chronic form the formation of tubercles is less obvious, the ulceration is indolent, while granulations and nodular thickening may cause it to resemble lupus. Pain, wasting and febrile symptoms are well marked; though, of course, concomitant pulmonary disease will be attended by the usual clinical phenomena.

Tuberculous disease of the tonsils occurs alone or in association with the palatine deposit. It manifests itself by congestion and enlargement of the glands, and superficial ulceration soon occurs, the ulcers being multiple and with irregular ill-defined margins; they are covered with grayish white muco-purulent matter which contains the specific bacillus.

The diagnosis of the acute form has to be made from diphtheria, follicular tonsillitis, syphilis, herpes, and small-pox; while the chronic variety must be distinguished from lupus and syphilis.

The presence of pulmonary lesions will, of course, at once suggest the probable nature of the throat affection, and the characteristic miliary tubercles and superficial "worm-eaten" ulceration will serve to exclude diphtheria, syphilis, and small-pox: the general symptoms will likewise differ from small-pox and diphtheria. In herpes of the fauces, the clear vesicles and absence of severe constitutional disturbance should prevent any mistake in diagnosis. In lupus, apart from the rarity of the primary faucial cases, the occurrence of slowly forming, clear, apple-jelly-like, painless tubercles and the tendency to cicatrisation of the clean ulcers should serve to distinguish it from the irregular ulcers of tubercle, which are covered with detritus and never cicatrise.

Treatment.—In all cases the affected tissues, having been cocainised, should be thoroughly scraped with a sharp curette, and lactic acid applied daily (20 to 80 per cent solution). In many cases the disease may be arrested, at least temporarily, by this method. In the acute form ice should be sucked and the throat frequently sprayed with a solution of cocaine (4 per cent) and menthol (20 per cent) in adepsine oil.

The general treatment should be the same as in pulmonary tuberculosis.

Syphilis of the pharynx.—Syphilitic disease may affect any part of the fauces and pharynx, and in the more exposed regions occurs in all stages—namely, i. Primary chancre; ii. Erythema; iii. Mucous patch (condyloma); iv. Superficial ulceration; v. Gumma; vi. Deep ulceration; vii. Cicatrix. Though it is generally possible to assign pharyngeal syphilis to the so-called secondary or tertiary periods, the statements made on this point in reference to laryngeal syphilis (see p. 806) apply, though to a less extent, here.

i. The primary sore, though decidedly rare in this region, has been observed in a good many cases, chiefly on the tonsils, very occasionally on the faucial pillars; for whereas the irregular surface and crypts of the tonsil form a ready means of entrance for the infection, the smooth unbroken surface of the fauces and soft palate affords but slight opportunity for inoculation; consequently, with very few exceptions, the essentially localised initial sore is encountered on the tonsils only, and generally in cases where the tonsils are already chronically enlarged.

The affected tonsil is red, and the sore is generally eroded, without marked ulceration, presenting a sharply-cut, well-defined margin, with a small amount of sticky, grayish white secretion covering the floor of the ulcer. There is very marked induration on palpation, often stony hardness. The sore often extends over the whole surface of the tonsil, and the submaxillary glands are very much enlarged and tender to pressure; but they do not suppurate. Pain is seldom well marked and is often absent; yet in some instances it is severe and lancinating in character.

ii. Erythema usually occurs between six weeks and four months after the initial sore, and is generally coincident with cutaneous erythema or the papular syphilide. It presents a peculiar, almost characteristic bright bluish red, symmetrical hyperæmia, generally confined to the soft palate and pillars of the fauces, rarely implicating the tonsils, with a somewhat sharply-defined border, so that the line of demarcation between the hyperæmia and normal mucous membrane is almost abrupt. This appearance should always lead to the suspicion of syphilis.

There are generally no symptoms sufficiently notable to attract the attention of the patient; some stiffness of the parts may be observed.

iii. Mucous patches usually appear about the fourth month after inoculation, but, as they are remarkably persistent, they may be observed some years after. While ordinarily coexisting with a papular cutaneous syphilide, they often appear when there is no general manifestation of the disease. Mucous patches are usually more or less bilaterally symmetrical, slightly elevated, bluish white patches on the fauces, tonsils, or posterior wall of the pharynx; they are attended with slight congestion and superficial abrasion.

iv. Superficial ulceration is especially prone to occur on both tonsils, forming remarkable symmetrical kidney-shaped ulcers, with a grayish white, ill-defined border. But the ulceration may be limited to the posterior surface of the soft palate and the rhino-pharyngeal space. It is one of the earliest manifestations of secondary syphilis, often preceding or accompanying the cutaneous erythema, and, like the latter, usually disappears very soon, without sore throat. On the other hand, it may persist and be followed by a more painful inflammatory sore throat.

v. Gumma is generally unilateral and single, and in the soft palate, pillars of the fauces, tonsils, and particularly in the posterior pharyngeal wall may appear as a smooth, uneven, red or angry-looking swelling, covered and surrounded by congested mucous membrane. It rarely gives rise to much pain, and frequently to none whatever; but a sense of fulness and discomfort in the part or a difficulty in deglutition attracts the first notice of the patient. Very soon its centre becomes yellowish and soft, and, pain being absent, the gumma often breaks down before the patient consults a medical man, when a typical deep crateriform ulcer, with steep margins and a base covered with sticky muco-pus and débris, is already formed.

vi. Tertiary syphilitic ulceration is always due to the disintegration of gummatous deposit. In the earlier cases these ulcers are most found in the soft palate, faucial pillars, or uvula; but tertiary ulceration occurring many years after the initial lesion more frequently affects the tonsils and posterior pharyngeal wall. A gumma may form on the posterior wall of the soft palate or in the naso-pharynx. In the former case very rapid perforation of the palate or dropping off of the uvula may occur if the actual condition has not been diagnosed and treated. In view of the frequently painless character of the affection it is therefore essential that the posterior surface of the soft palate should be inspected by the rhinoscope, especially when the anterior surface appears red and infiltrated. Not only may the soft palate and uvula completely disappear, but the destructive process may involve the hard palate and open into the nasal passages.

vii. Cicatrix.—Deep syphilitic ulceration is generally followed by contraction, distortion, and adhesion of the tissues involved: thus the soft palate may be bound down to the posterior pharyngeal wall, more or less completely shutting off the rhino-pharyngeal space; or the uvula may become adherent to the faucial pillars. Syphilitic scars may often be recognised by their stellate or radiating appearance due to the contraction and dragging of neighbouring tissues towards the former site of the ulcer as a centre. A similar process occurring in the lower pharynx or œsophagus may lead to obstruction to the passage of food.

Inherited syphilis.—Inherited syphilis affecting the pharynx generally manifests itself in early infancy or at the age of puberty. It may assume the form either of secondary or of tertiary lesions, of syphilitic catarrh, erythema and superficial ulceration, or gummatous deposit with deep ulceration. Syphilitic catarrh and superficial ulceration are generally associated with a similar condition in the nasal passages, giving rise to what is commonly called "snuffles." Deep ulceration of the fauces or pharynx is very frequently combined with destructive ulceration of the nasal bones, as has already been described as a consequence of tertiary manifestations in acquired syphilis.

Diagnosis.—A tonsillar chancre is liable to be mistaken for tertiary ulceration, epithelioma, or tuberculous disease. From tertiary ulceration it is distinguished by its superficial character, the stony hardness of the tonsil, and the large cervical bubo; while the early appearance (in from two to four weeks) of secondary cutaneous manifestations will always settle the question. It is less easy to distinguish between a chancre and epithelioma, and very often it is impossible to do so till other syphilitic phenomena arise; but the duration of the affection, and the fact that the margins of the ulcers are flush with the surrounding tissues, which in turn are congested, will favour the diagnosis of chancre. The patient's age must also be taken into consideration. Malignant disease of the pharynx hardly ever appears before the age of thirty-five. The effects of mercurial treatment, and, finally, the microscopic examination of a fragment of the ulcerating tumefaction, will assist us in arriving at a definite diagnosis. Tuberculous ulcers are more irregular, they present a mouse-nibbled appearance, they are covered with copious sticky muco-pus, and are usually multiple. The enlargement of the cervical glands is less rapidly developed, and the evening rise of temperature and increased frequency of the pulse, even in the absence of concomitant pulmonary lesion, should lead to an examination of the débris for the specific bacilli.

Mucous patches and condylomata may be taken for diphtheria, from which the absence of constitutional symptoms and the presence of coexistent syphilitic skin disease should distinguish them. As a rule, the bluish white, symmetrical, opalescent appearance of the mucous patches surrounded by apparently healthy mucous membrane is in itself sufficiently characteristic, for the tertiary syphilitic ulcer seldom causes difficulty in diagnosis; yet the deep ulcer with foul-smelling disintegrated débris sometimes closely simulates a breaking-down epithelioma, from which it is distinguished by the red areola surrounding the margin, by the edge of the ulcer not being raised, and by the absence of the fungating base. In doubtful cases a microscopical examination of a fragment, and rapid diminution in size of the "growth" under iodide of potassium, would probably reveal the true nature of the case.

A gumma is sometimes diagnosed as quinsy, especially when its formation is attended with pain and febrile symptoms; or it may be mistaken for a fibroma, sarcoma, or carcinoma. In the former case the facts that it is unilateral, little tender to pressure, not painful, and not inflamed on the mucous surface, favour the diagnosis of gumma. Fibroma is very rare, but in doubtful cases antisyphilitic treatment must be relied upon to distinguish both this and malignant growths from gumma. Sarcoma is less rapid in growth, and presents a more highly coloured and succulent aspect.

Treatment.—Mucous patches which do not disappear with anti-syphilitic remedies may be painted at intervals with a solution of nitrate of silver (20 grains to the ounce). This, however, will be very rarely required. Superficial ulcers may be painted with solution of chromic acid (grs. x. to the ounce); the ulcerated surface must previously be wiped dry.

Deep ulcers should be cleaned by a simple alkaline gargle or spray, and a mercurial antiseptic gargle used afterwards.

Cicatricial stenosis of the rhino-pharynx may require division with subsequent dilatation persistently repeated for a long time; as all syphilitic scars tend to contract afresh.

The general treatment of syphilitic disease of the pharynx does not differ from the treatment of similar manifestations in the larynx, to which the reader is referred (p. 811). The remarks there made on the necessity of avoiding too rigid an adherence to any routine method of treating secondary lesion with mercury, and tertiary lesions with iodine of potassium, apply with equal force to syphilitic disease of the pharynx.

Local treatment is usually unnecessary; but in all syphilitic affections of the pharynx an antiseptic gargle, such as a solution of perchloride of mercury (1 in 1000), may be used with advantage.

Gouty affections of the throat.—The so-called "lithæmic diathesis" is a much more frequent cause of throat disease than is generally believed. This is probably largely owing to the fact that the throat is often affected in patients who present no definite evidence of gout, or who have never had any acute joint inflammation.

Symptoms.—The throat manifestations of gout may assume the acute or chronic form.

Acute gouty pharyngitis, tonsillitis, or laryngitis may result from exposure to cold, or may occur without any obvious local cause in predisposed persons. The affection may run the usual course of acute inflammation of these regions, or may yield abruptly to an ordinary attack of acute gout. One of us (W. W.) observed a case of a medical man, who had had many definite attacks of gout, in which nocturnal laryngeal spasms were prone to occur whenever an error in diet rendered the patient gouty. A similar case was observed by the editor of this work; in this case, in a fine and vigorous but gouty man of middle age, the spasms, which recurred at intervals for some years, would compel the sufferer to spring from his bed in an agony: the local signs were never very notable. The chief distinguishing subjective symptom is that the pain, or spasm, is out of proportion to the degree of inflammation.

Objectively the fauces or larynx, as the case may be, are acutely inflamed and bright red, the inflammation, as a rule, being strikingly patchy in appearance; the inflammation is particularly noticeable on the lateral pharyngeal walls, while the uvula may be œdematous.

The more chronic form may be indistinguishable from ordinary pharyngitis and laryngitis; but in most cases there is well-marked thickening of the lateral walls of the pharynx. As indicative of gout we lay particular stress on lateral pharyngitis with a sense of uneasiness or pain on swallowing; the pain may be of a darting character and shoot up to the ears. Small tophi may form under the mucous membrane and may be expelled; or urate of soda may be discharged from accumulations in the mucous membrane. These gouty concretions, in exceedingly rare instances, may form on a vocal cord (as in a case recorded by Virchow), or within the crico-arytænoid joint, causing anchylosis. A gouty inflammation of such character may produce symptoms and physical signs indistinguishable from those of laryngeal cancer. In a case seen by one of us (F. S.) in consultation, thyrotomy was performed by a distinguished surgeon on suspicion of malignant disease of the larynx; but the supposed new growth turned out to be a gouty concretion embedded in a vocal cord. A similar instance came before Krishaber and Morell Mackenzie; in this case the laryngeal disease disappeared while the patient was undergoing treatment for gout.

The diagnosis of gouty affections of the throat is often simple enough if the peculiar patchy aspect of the inflammation and the lateral pharyngitis are noted. Such appearances, especially when attended with unusual sensitiveness and pain in the throat, should lead to inquiry into the family and personal history of the patient, and to careful investigation into any constitutional or other local manifestations of the gouty habit; in many instances, however, the diagnosis must largely depend on the response to suitable treatment. On the other hand, it does not by any means necessarily follow that every inflammatory affection of the throat in a gouty patient is itself of gouty nature.

The treatment is simply that suited for systemic gout, the only local treatment necessary being some sedative spray or pastil containing menthol and cocaine. Tincture or wine of colchicum (♏ x. to ♏ xxx.), with or without bicarbonate of potash or salicylate of soda, may be added to a tumbler of Vichy water and taken twice daily after meals, in the more chronic cases a visit to some appropriate spa is highly to be recommended to patients of sufficient means and leisure. The more acute cases should be treated as acute attacks of gout, and in the usual manner, the patients being confined to the house.

Under any circumstances the larynx, if inflamed, should be rested as much as possible, and all sources of irritation removed; and, after the gouty condition has been combated by appropriate treatment, the treatment suited to subacute or chronic inflammation of the pharynx or larynx may be necessary.

Needless to say, the usual dietetic rules for gout must be strictly carried out.

Rheumatic affections of the throat.—The causes of rheumatic affections of the throat differ in no respect from those of rheumatic affections occurring in other parts of the body; nor can it be said that there are any distinguishing characteristics of rheumatic pharyngitis, tonsillitis, or laryngitis. The very intimate pathological connection between acute lacunar tonsillitis, peritonsillitis, and acute rheumatism is now widely recognised; but it is important to remember that a large proportion both of acute and chronic pharyngitis and laryngitis is of rheumatic origin, for success in their treatment will very much depend on a correct diagnosis. Pain, stiffness, and inflammation of the fauces very frequently precede an attack of acute rheumatism, and either subside or are disregarded when the acute joint symptoms are manifested. In other cases the throat symptoms persist for days or weeks without further development, and not seldom recur regularly whenever the patient is exposed to cold or damp. Rheumatic inflammation may arise in and around the crico-arytænoid joints, or directly attack the intrinsic muscles and peripheral nerves, causing diffuse neuritis, impairment of mobility of one or both vocal cords, and in some cases marked tenderness to pressure. The diagnosis of "rheumatic" paralysis of the vocal cords, however, ought not to be made until after exclusion of all other possible *organic* causes of the palsy.

Treatment.—It is unnecessary to suggest the general treatment to be adopted in rheumatic affections of the throat, for it is simply that suited to rheumatic diseases of the joints. Locally a sedative spray, such as menthol and cocaine in colourless oil of vaseline, and other local treatment referred to in the chapters on acute and chronic inflammation of the pharynx, tonsil, and larynx, should be carried out.

New growths of the pharynx and tonsils.—A. *Benign Neoplasms.*—It is as little possible in the present state of knowledge to assign any definite cause for the appearance of benign neoplasms in the fauces as elsewhere, with the sole exception of dermoid tumours, which very rare growths are abnormalities of development.

Benign growths are not of frequent occurrence in the fauces. *Papilloma* is by far the most common form; the small, warty, sessile or pedunculated, light pink growths, with cauliflower or granular surface, being usually attached to the margin of the soft palate, the pillars of the fauces, or the uvula. Next in point of frequency comes the *adenoma*, a hard, rounded, sessile growth of slow development, covered with smooth, irregularly rounded mucous membrane of normal appearance, arising in the mucous membrane of the anterior or posterior surface of the palate or in the tonsil, and often attaining a considerable size. Fibroma is very rarely met with in the fauces, though it is more common in the rhino-pharynx, where as a rule it is attached to the vault of the pharynx. These tumours are somewhat rapid in their growth, and may become as large as a hen's egg or a small orange. They are hard, rounded, smooth and red on the surface, and sometimes highly vascular.

Angioma may occur as purple, nodular, soft, vascular growths, composed of enlarged tortuous blood-vessels held together by a small amount of connective tissue. Calcareous concretions occur in the tonsil and rarely in the soft palate, and, being covered by mucous membrane, the swelling may simulate a growth.

Diagnosis.—Papilloma often bears a very strong resemblance to a warty epithelioma. There is generally no infiltration of the neighbouring tissues, and no zone of hyperæmia around the benign neoplasm; but a microscopical examination of the removed growth should always be made.

Fibroma and adenoma are very similar in aspect and consistence, but the former are much rarer than the latter, and develop more rapidly.

Prognosis.—The prognosis as regards life is always favourable; and the same may be said of the results of operative interference, as they do not tend to recur after radical removal.

The *symptoms* manifested by all these benign growths are mainly due to mechanical interference with the action of the soft palate, with deglutition and phonation, or, if very large, with respiration; and the severity of the symptoms depends chiefly on the size of the growth. A papilloma on the tip of the uvula may give rise to the usual symptoms of elongated uvula. Fibromas are sometimes rather painful, especially if large; and, like any large growth in this region, may give rise to a sense of fulness and discomfort.

Treatment.—A papilloma should be cut off, and the tissues immediately around the seat of attachment included in the excised portion. An angioma may be removed by the galvano-cautery snare; but hæmorrhage is apt to be considerable if precautions are not taken to prevent it. The other forms of growth should not be removed unless their presence occasion inconvenience or pain. Fibroma, especially of the rhino-pharynx, may give considerable trouble in removal. A description of the many surgical methods employed to overcome this difficulty is outside the scope of this work.

B. *Malignant Neoplasms.*—Both carcinoma and sarcoma occur with tolerable frequency in the fauces and pharynx.

The causes of malignant growths in this region are as obscure and ill-defined as are the causes of similar growths occurring in other parts of the body; heredity and local irritation seem to exercise some influence in their occurrence. Almost invariably the pharyngeal growth is primary, or due to extension from neighbouring structures; malignant disease in this region is very rarely secondary or "metastatic."

The male sex is more frequently attacked than the female; especially is this the case with carcinomatous growths. It is rare for carcinoma to appear before the age of forty, and the great majority of all forms of malignant disease of the pharynx do not begin till after the fifth decade; sarcoma, however, may occur at any age.

Pathology.—The morbid anatomy of growths occurring in the pharynx does not differ in any way from the usual structure of similar growths in other regions. Primary carcinoma either occurs in the soft palate or pillars of the fauces, the tonsil, rhino-pharynx, or the lower pharynx at its junction with the œsophagus.

If arising in the soft palate it generally soon spreads to the tonsil, or from the pillars of the fauces to the tongue; while carcinoma of the lower pharynx tends to involve the larynx, so that it is often impossible to define the seat of origin. The growth presents an uneven surface and soon ulcerates. In its earlier stages epithelioma usually appears as a wart-like growth surrounded by hyperæmic, infiltrated tissue. At first it grows rather slowly, but, as it attains a considerable size, it rapidly spreads, involving surrounding structures in all directions. The growth sometimes forms a large tumour; but in other cases it soon begins to break down in the centre, the ulceration extending laterally as well as in depth, fresh nodules forming in the immediate neighbourhood of the hard, elevated margin, soon to be included in the ever-advancing ulceration. The base of the ulcer is covered with muco-pus and breaking-down tissue, in the midst of which uneven ridges of the growth and ulcerating nodules are seen; but no granulation tissue is formed and scarring never takes place. The glands of the neck, and particularly those under the angle of the jaw, are soon extensively involved, whether the growth arise in the fauces or rhino-pharynx; when the laryngo-pharynx and œsophagus are the primary seat, the cervical glands are not so rapidly implicated.

The varieties of sarcoma met with in the fauces and pharynx comprise lympho-sarcoma, round-celled sarcoma, mixed round and spindle-celled, spindle-celled, alveolar, melanotic, and myxo-sarcoma. Lympho-sarcoma is probably the most common variety, and Mr. Butlin has suggested that a connection probably exists between this form of growth in the fauces and Hodgkin's disease; and that in some cases the primary lymphoid deposit occurred in the faucial lymphatic tissues. While it is beyond dispute that many cases of sarcoma of the fauces and tonsil display a mild malignancy, and that instances occur in which the faucial lymphoid tissue becomes involved in the course of Hodgkin's disease [*vide* p. 579], it is most unusual to see the latter affection following the appearance of sarcomatous growths in the fauces. Kundrat ha observed lympho-sarcoma in two cases of pseudo-leukæmia; Chiari state that leukæmia and pseudo-leukæmia are distinguished from lympho sarcoma of the throat by the infection of the lymphatic glands of th whole body as well as of the spleen and liver. Sarcoma grows somewhat rapidly; and when the growth has attained any size, the mucou membrane covering it is succulent and bright red in aspect, and i infiltrates and displaces the neighbouring structures. It begins in th tonsil, or in a lymphoid follicle of the mucous membrane of the so palate, pillars of the fauces, or rhino-pharynx. It is less hard tha epithelioma, and sometimes is soft and gives the sensation of a cyst abscess. The rate of growth varies a good deal; in some cases remains localised for a considerable period, or for a time may diminis in size. It spreads by extension to the neighbouring regions, and ve generally involves the deeper tissues behind the angle of the jaw, so to cause large swellings in the neck; sarcomas in the fauces or tonsil, the contrary, not infrequently remain distinctly localised and more or l encapsuled for a long time, and then it is only when they extend beyo the limiting capsule that they increase rapidly and involve neighbouri structures and glands. Ulceration does not occur very early, and when it does it is usually superficial, and hæmorrhage very slight.

Lympho-sarcoma of the throat is a rare affection, and generally occurs in middle-aged men. O. Chiari, who has made a special study of this variety of pharyngeal growth, states that it arises either on one of the tonsils or in the lymphoid follicles of the soft palate or rhino-pharynx; or the lymphatic glands of the throat, mostly on one side, may be attacked, and from them conical tumours may grow towards the throat, causing more or less narrowing of the space. Lympho-sarcoma appears either as a definite tumour on the tonsil or as an infiltrating growth; in either case ulceration and breaking down of the surface soon occur.

Thus the larger tumours or the flat complex of smaller growths break down or suppurate. The resulting ulcers may heal partly or entirely, and even deep scars may be formed; yet soon fresh points of infiltration appear on the edge of the old ulcer, either as yellowish marrow-like nodules or simply as diffuse thickening. In this way the process spreads superficially. Sometimes the degeneration and the breaking-down process are accompanied by febrile disturbance. Like other forms of sarcoma, the lympho-sarcomatous tumour may, temporarily, diminish in size.

Symptoms.—Carcinoma of the fauces is usually accompanied by pain of gradual onset, increased but not induced by deglutition, and lancinating in character, darting up to the ears. Salivation is often present. The voice becomes throaty or nasal in quality. A large growth may produce considerable dysphagia. Difficulty in swallowing, indeed, is often the earliest and most marked symptom in growths occupying the laryngo-pharynx; obstruction to nasal respiration and a sanious muco-purulent discharge occur rather when the rhino-pharynx is the seat of the disease. The breath becomes fœtid when the tumour breaks down, and cachectic symptoms are seldom long delayed. In sarcoma and lympho-sarcoma the symptoms generally consist chiefly of mechanical obstruction to respiration and deglutition, and alteration in the quality of the voice. Pain is not usually a marked symptom, though generally noticeable when superficial ulceration has occurred. With the further progress of the growth deep ulceration with foul muco-purulent discharge, quickly-increasing extension of the disease, pain, loss of appetite and general weakness become manifest, and the patient then rapidly sinks.

Diagnosis.—The differential diagnosis of these forms of malignant growths often presents many difficulties: first, in distinguishing between the different varieties of malignant growths, a point of importance as regards prognosis and the advisability of operative interference; and, secondly, in distinguishing them from benign growths and various infective diseases.

Carcinoma differs from sarcoma in the early onset of pain, its irregular surface and infiltrating character, and the rapid secondary infection of the neighbouring glands; early fixation of the lower jaw and the early appearance of cachectic symptoms being in favour of carcinoma. The growths are usually harder on palpation, pale pink or even bluish pink in colour, and are surrounded with a well-marked areola. Ulceration and hæmorrhage occur early; the margin of the ulcer is ulcerated, raised, and irregular, and the floor is covered with characteristic cauliflower vegetations. A sarcoma is softer, smoother, and more succulent in aspect, covered with light pink or yellowish pink mucous membrane, and ulceration is often delayed. The ulceration tends to remain superficial, but when the growth does break down there is a copious secretion of ichorous muco-pus.

Lympho-sarcoma differs from sarcoma and carcinoma in that these arise as more or less globular tumours, the ulceration of which shows less tendency to spread on the surface. The lympho-sarcomatous ulcer is thickly covered with ichorous pus, but the floor shows no cauliflower excrescences. Moreover, the lympho-sarcomas show greater tendency to diminution; and the ulceration often heals, at any rate for a time.

In all forms a microscopical examination of removed fragments of the growth will generally decide the question of diagnosis; but it is necessary to proceed in this research with great caution: first, we must obtain a piece which includes the deeper tissues of the tumour, for superficial portions may only show normal or inflammatory tissue without evidence of malignancy; and, secondly, we must distinguish between the varieties of carcinoma which closely resemble sarcoma.

The diseases most likely to be mistaken for malignant growths, and conversely, are chronic hypertrophy of the tonsils, tonsillitis, benign growths, syphilis, tuberculosis, lupus, diphtheria, and chronic retropharyngeal abscess. Chronic hypertrophy of the tonsils is almost invariably bilateral, and is essentially a disease of early childhood and adolescence, and although enlarged tonsils dating from childhood may persist throughout life, yet an enlargement beginning in an adult, especially if unilateral, must always be regarded with grave suspicion.

A sarcoma may be mistaken for gumma, and especially for a gumma which looks yellowish and marrow-like just before breaking down; the only trustworthy distinction, indeed, consists in the failure of syphilitic medication. An ulcerating sarcoma, especially if ulceration be attended with febrile disturbance, may resemble acute tonsillitis, or peritonsillitis; but the more gradual onset, slight constitutional disturbance, and absence of acute pain or tenderness, would serve to distinguish these affections apart from the aspect of the growth. Sometimes an ulcerating sarcoma, and more especially a lympho-sarcoma, is covered with a thick layer of muco-pus which may simulate diphtheria or syphilitic ulceration. The presence of fresh nodules of growth around the margin, the shape of the ulcer, and the fact that it is always single, together with the general condition and freedom from albuminuria and from characteristic bacilli in a culture, would point to a malignant growth.

Syphilis is more likely to be diagnosed when a malignant growth has undergone extensive breaking down with deep ulceration. Very often only a microscopical examination of a removed fragment and the administration of iodide of potassium will settle the question. Yet it is always important to remember that a temporary subjective amelioration, and even a transient diminution in the size of a malignant growth, may be produced by the exhibition of iodide of potassium. Too much stress ought not to be laid on the history of a syphilitic affection, or evidence of old syphilitic scars, and the like; for, on the one hand, in syphilis a history of infection is often unobtainable, and on the other hand malignant disease not infrequently occurs in syphilitic subjects.

The peculiar apple-jelly-like nodules of infiltration around lupus ulcers should prevent an error in diagnosis as regards this disease.

Similarly ulcerating sarcoma may bear a strong resemblance to tuberculous ulceration; more especially is this true of lympho-sarcoma. Tuberculous ulcers are more superficial, have mouse-nibbled edges, and are usually multiple. If no concomitant pulmonary symptoms are detected, the examination of the muco-purulent secretion will reveal the tubercle bacilli; while the frequent pulse and nocturnal rise of temperature should lead to a suspicion of this disease. Of course the presence of pulmonary tuberculosis does not exclude the possibility of a malignant tumour in the pharynx.

A warty epitheliomatous growth on the fauces may closely resemble a benign papilloma; yet it differs from it in growing from an indurated base, and in being surrounded by a zone of hyperæmia and infiltrated tissue. Similar points of distinction serve to differentiate malignant growths and fibroma; but a sarcoma may appear so truly benign in aspect, in rate of growth, and in the absence of any enlargement of neighbouring structures and glands, that the only means of diagnostic distinction may be in a microscopical examination of a removed fragment (the possible sources of error will be fully discussed in the chapter on malignant disease of the larynx, p. 839). The same difficulty may arise in the distinction of the rarer forms of benign growth, such as adenoma, and malignant growths.

Chronic retropharyngeal abscess occurs in an unusual site for sarcoma, and presents a smooth swelling which fluctuates on digital exploration, and is sometimes associated with cervical caries. Aspiration of the tumour would, of course, reveal its true character at once.

Prognosis.—The prognosis of carcinomatous growths in the pharynx is very grave. To this statement an exception may be made in the case of small warty growths which appear on the soft palate or uvula, and which may be radically extirpated in an early stage.

A sarcoma occurring in the fauces is a more hopeful affair, especially the less rapidly-growing spindle-celled variety and the lympho-sarcoma. These growths may remain encapsuled for a long time, so that a relatively favourable prognosis is justified when secondary extension is slow to appear, inasmuch as a radical operation is often completely successful. It is hardly necessary to say that any form of malignant growth, especially in a region so difficult of access as the tonsils or fauces, not to mention the rhino-pharynx, is peculiarly grave; but on the other hand there is too great a tendency to overlook the fact that many recorded cases prove that a radical operation has been completely successful, especially of late years; and from personal experience we would emphasise the importance of not regarding malignant disease in this region as invariably hopeless.

Treatment.—From a therapeutic standpoint the importance of early diagnosis and early radical removal of malignant growths cannot be too strongly emphasised; for once the growth has extended beyond the structures which permit of complete removal, or has affected the neighbouring lymphatics, it is hardly possible to hope for lasting cure; whereas, as has already been stated, early and complete extirpation—especially of late years—has produced most brilliant and permanent results. In considering the advisability of attempting a radical operation, the surgeon will be guided not only by the situation and limitations of the growth, but also by the particular variety of malignant tumour to be dealt with; for an encapsuled or well-defined sarcoma, especially if it be a lympho-sarcoma or a spindle-celled sarcoma, may be permanently removed, although a similar procedure in the case of encephaloid cancer would probably be unsuccessful.

The choice lies between removal through the mouth by the knife, snare, or ecraseur, and lateral pharyngotomy. One of us (F. S.) has seen several very successful cases of early operation from the outside.

It is impossible, however, to lay down rules for guidance in every case; each has to be judged on its own conditions.

On the other hand, growths may require partial removal when there is danger of suffocation or difficulty in swallowing; and pharyngeal or œsophageal constriction may necessitate gastrostomy or lateral œsophagotomy.

When a radical operation is impossible, or has been followed by recurrence of the growth, all that can be done is to maintain the patient's strength by nourishing diet and suitable tonics, and to alleviate pain by opium. Ulcerating growths should be cleansed with antiseptic sprays and gargles.

DISEASES OF THE RESPIRATORY ORGANS

GENERAL PATHOLOGY OF RESPIRATORY DISEASES

In this chapter a short account will be given of the action of the mechanism of breathing, in health and in disease, and also of certain phenomena which commonly occur in the course of respiratory diseases, and which are partly concerned in their pathology: such incidents as cough, dyspnœa, and asphyxia; the carbonisation, so-called, of the blood; and, in each case, the results of these actions, as seen in the lungs and in the general system, will be traced. With regard to these subjects, it is needful to call attention to the peculiar structure of the lungs, and to their relations with other parts of the frame.

The lungs are, to some extent, set apart from the rest of the body. Suspended from the trachea and blood-vessels, they are indeed connected with the general system by vessels and nerves, and by the mucous membrane; but, under normal conditions, they are kept in apposition with the walls of the thorax by atmospheric pressure only. They have a separate heart, and special muscles to control the influx and efflux of the air. As Claude Bernard was fond of repeating, they are an artifice of construction, by which an animal, otherwise aquatic, can exist and move in the open air. "Les tissus vivans sont aquatiques sanguinaires, ils se repaisent du sang dans lequel ils sont plongés. Ils y vivent comme des animaux aquatiques" (2).

Again, no organ in the body contains such a variety of structural elements as the larger-sized bronchial tubes. Both large and small tubes are provided with an epithelium, an inner connective layer, a circular muscular layer, and a well-marked outer fibrous tissue layer; and the larger have, in addition, a compound epithelial layer, a well-marked basement membrane, hyaline cartilages, and mucous glands. In consequence of this complication of structure, and of the relations existing between the lungs, heart, and brain, it follows that all long-continued affections of the pulmonary organs have an extremely complex pathology. Yet in most respiratory disorders, in spite of their great complexity, there is much in common; certain disturbances of the normal functions of the body which arise during their course are closely similar, and these, notwithstanding much difference in the modes of their inception, often bring in their train a series of related changes between the central and remote portions of the frame which in their final results are strikingly alike.

In illustration of this statement we may compare the results of certain serious diseases of the lungs with those that have, at the outset at any rate, a comparatively trivial origin.

The more serious diseases of the lungs are usually the result of inflammation due to some irritant; this, if repeated or long continued, impairs the lung-tissues, and may do permanent damage to the heart and nervous system. It matters very little that these actions may have been produced by different causes—by the direct influence of heat or cold, by mechanical or chemical agents, by micro-organisms or their products—the consequences will often be very similar. The struggle of the elements of the animal body to overcome or to remove the sources of irritation, to clear away the effects of their presence, or to buttress the tissues against them, may entail structural changes in the lungs themselves of more or less gravity; but they also often lead to cough, dyspnœa, and ultimately to serious consequences in distant organs.

On the other hand, a simple mental disturbance, as in hysteria, a strong emotion, or a purely reflex irritation, as in certain forms of ear-disease, or an intestinal irritation, may excite the respiratory centre in the medulla and induce dyspnœa; or again, these accidents may cause a violent spasmodic cough, which, in certain weakened conditions of the lung-tissues, may do serious injury to the system.

The similar results which arise from these special factors we are presently to study; and, in the first place, it is important to note the mode of action of the ribs and of the muscles acting upon them.

The mechanism of breathing.—In healthy breathing a large part of the inspiratory act is accomplished, both in men and women, simply by the contraction of the diaphragm; and expiration takes place, as soon as this muscle is relaxed, by means of the natural elasticity of the lungs. The extent of movement of the ribs in these actions is very small, especially in the upper parts of the chest,—a fact we may note at any time by watching the tranquil breathing of a healthy person during sleep.

The natural stimulant of the respiratory centre in the medulla is the carbonic acid of venous blood; and when the need for oxygen has been satisfied by inspiration, the inhibitory action of the vagi brings about the act of expiration. But as soon as, from any cause, such as extra exertion, the oxygen tends to fall below the normal, or the carbonic acid to rise above it, the automatic action of the vagi comes more strongly into play, and forces the breathing.

In forced breathing not only the diaphragm, but the intercostals, the scaleni, and other accessory muscles also, come into action; and the ribs begin to play an important part, both in inspiration and expiration.

Not only are these bony levers raised during inspiration, and lowered during expiration, but in the final forced efforts at expiration there is also a distinct shortening of their chord-lengths.

The flexibility of the living rib, and its liability to be bent, even permanently, is shown clearly enough by the sinking in of the thoracic wall over the site of a dried-up vomica; when the lung does not expand on the absorption of pleuritic fluid; by the barrel-like distension of the chest in emphysema; by the indrawing of the lower ribs in dyspnœa; and by the deformity of the rachitic thorax.

FIG. 11.—Thoracic callipers

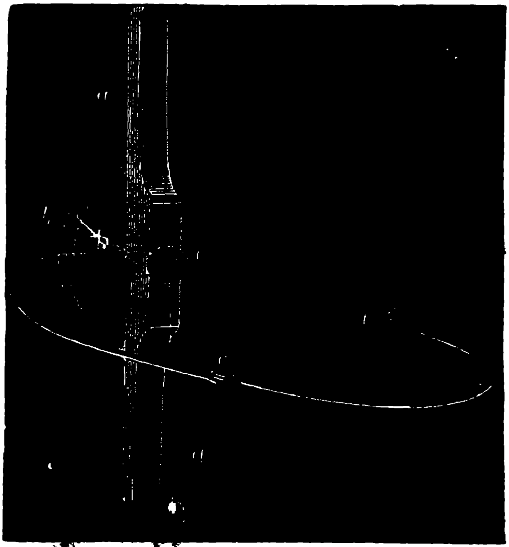

FIG. 12.—Rib goniometer.

In forced expiration the inbending of the ribs has been demonstrated by the following means:—[1]

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[1] A full account of the investigations on this point will be found in the author's work *Stethometry*, published by Macmillan, London, 1876.

(i.) By actual measurement of the chord-lengths of the ribs, after full inspiration, and again after forced expiration, by means of the thoracic callipers (Fig. 11). (ii.) By calculation of the *possible* extent of motion of the ribs, considered as rigid levers; the angles made by the plane of the ribs with the vertical being ascertained by means of a specially designed goniometer (Fig. 12). (iii.) By a comparison of the extent of forward and upward movements of the anterior ends of the ribs in young children, in adults, and in old people. The forward motion is in proportion to the flexibility of these levers. (iv.) By the explanation which this bending of the ribs affords of the measurements of the movements of the chest wall in various diseases, and of the deformities produced in the thorax by such diseases as whooping-cough. The cyrtometer shows the extent of these deformities clearly enough. (v.) By the shape of the tracings, made with the stethograph, of the course taken by the anterior ends of the ribs, in forced breathing, and in the various acts of coughing, sneezing, and yawning; and by the differences in the rib-tracings of movements voluntarily produced.

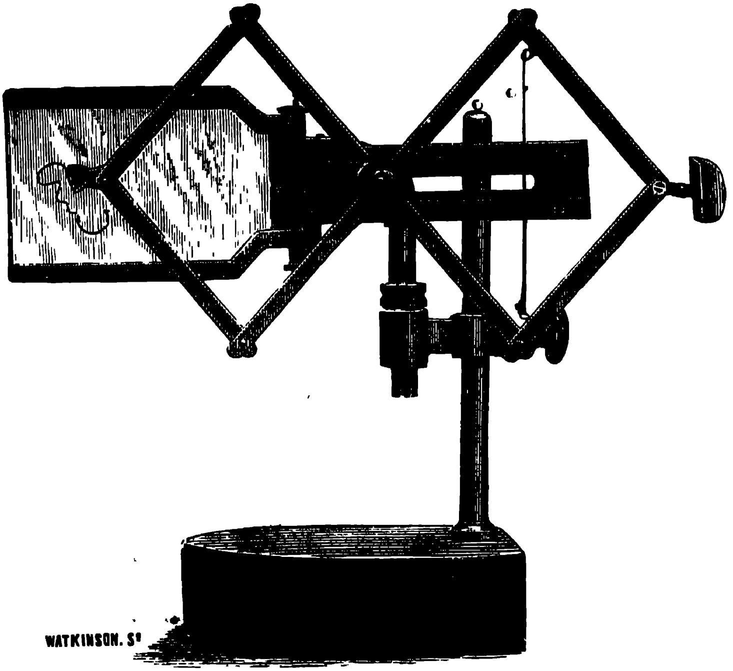

FIG. 13.—Two-plane stethograph.

The last-named method has so important a bearing upon our present subject that it will be briefly described.

The action of the stethograph will perhaps be sufficiently shown by the accompanying diagram (Fig. 13).

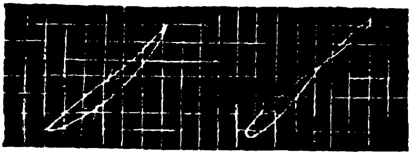

Fig. 14.—Movement of the clavicle in a healthy man, æt. 39

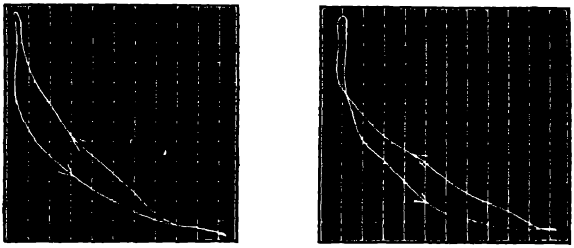

Fig. 15.—Movements of the third ribs in a healthy woman, æt. 29.

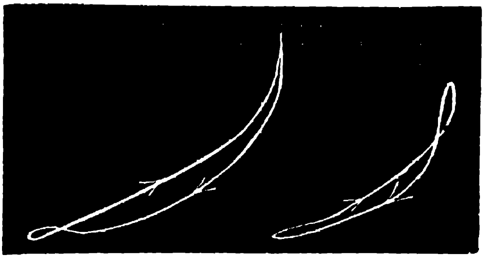

Fig. 16.—Healthy adult man. Movements of third ribs.

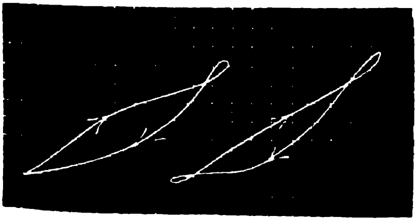

Fig. 17.—Same case fifth ribs.

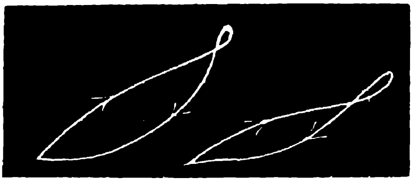

Fig. 18.—Same case, seventh ribs.

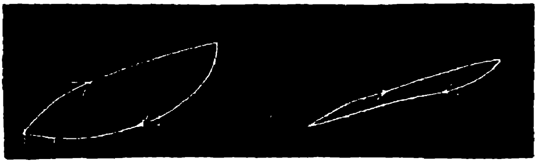

Fig. 19.—Same case, eighth ribs.

The tracings are taken by supporting the back, by means of a pad placed opposite to the spinal articulation of the rib under examination. The button of the stethograph is then kept in apposition to the anterior end of the rib, and the pen is adjusted to the screen, which, in the more delicate experiments, may be of smoked glass or of paper; it is divided into squares of $\frac{1}{10}$th inch of side.

The preceding curves (Figs. 14-19) are selected to illustrate the results, but I shall do no more now than just advert to the proofs they afford of the elastic property of the rib-levers themselves.

In these rib-tracings a steady increase in the degree of horizontal compared with the vertical motion is apparent, from the clavicles to the eighth ribs; and in all there must have been a considerable indrawing of the anterior ends of the ribs in forced expiration.

Acts of forced breathing, such as we have now surveyed, are, in health, only temporary. As soon as the occasion passes the respiration returns to its former tranquil character.

But in most respiratory disorders, at any rate during a portion of their course, the movements of breathing, although diminished on the whole, yet approximate to the forced type; in other words, to a true dyspnœa: and, usually, an entirely new set of actions is also introduced—the spasmodic, or, as Cohnheim appropriately calls them, the "explosive" expiratory impulses of sneezing and coughing.

It will be convenient to take the latter set of actions first, both because of the assistance that we shall gain in their study from the stethographic tracings; and because cough, for the most part, precedes the subsequent dyspnœa, and is often the cause of it.

On coughing and sneezing.—The primary intention of these acts is doubtless the removal from the air-passages of matter lodging in them and irritating the sensory nerves.

When the source of irritation is in the mucous membrane of the nose, sneezing is usually the result, the sensory fibres of the fifth pair of nerves conveying the impulse to the brain.

When the offending body is in the larynx, or near the epiglottis, the wave of sensation follows the superior laryngeal nerve.

The posterior wall of the larynx seems to be a very sensitive part, but the trachea is also easily irritated, and, again, both sneezing and coughing may be started by reflex irritation from regions outside the respiratory apparatus. In disease this sensitiveness is often greatly increased, owing both to causes in the bronchial mucous membrane itself, and to external impulses, such as exposure of the skin to draughts of cold air. On the other hand, after repeated irritations, there may be a diminished sensibility of the parts, as in snuff-takers; or after repeated catarrhs; and, usually, in bronchitis, secretion must reach a certain quantity in order to excite coughing, and must, moreover, come into contact with some sensitive spot in the bronchial tubes.

This sensitiveness of the mucous membrane is of considerable importance, since, if it be absent, or if the rima glottidis be kept permanently open by any cause, foreign bodies can penetrate into the inmost part of the lungs, and set up much mischief.

This accident happens not infrequently in cases of coma, or in paralysis of the adductors of the vocal cords; and it must be remembered that after the foreign body has passed the bronchi, its irritation will no longer excite the act of coughing. Vagus pneumonia, as it is called, which follows section of the vagi in the rabbit, often arises in this manner. Often, too, the particle thus entering may be too small, or too unirritating to cause cough; thus, fine coal-dust may lodge in the textures of the lungs and give rise to anthracosis. Other pneumonoconioses arise in a similar fashion; but, in the case of sharp and irritating dusts, there is another safeguard in the outpouring of mucus from the mucous membrane. This envelops the particles, and by ciliary action they are carried up to the more sensitive parts of the air-passages, where they are expelled by cough. This safeguard, however, often fails, and then, as in occupations involving the constant inhalation of such irritating particles, cirrhotic conditions of the lungs supervene [*vide* art. "Pneumonoconiosis," vol. v.] Similar remarks apply to the inhalation of putrefactive and pathogenetic bacteria. The former, if they escape the mucus, and are not discharged by cough, may remain embedded in stagnant secretions, and may give rise to putrid instead of simple bronchitis, or even to gangrene of the lung. Phthisis is usually the consequence of the inhalation of tuberculous dust, and other specific poisons probably enter the system through the air-passages.

Mechanism of the actions.—In *sneezing*, after inspiration, there is no complete closure of the air-passages, but a sudden, swift effort of expiration.

In *coughing*, the preliminary inspiration is followed by more or less complete closure of the glottis; then, by a sudden expiratory effort, the air in the chest is compressed, the block at the larynx is suddenly lifted, the ribs rapidly descend, are drawn downwards and inwards, at their anterior ends, so as to compress the lungs, and the air is forced at high pressure through the upper air-passages. The action is something like that of a pop-gun; and the offending material is usually thus expelled from the larynx, and often into the mouth. This sudden and energetic effort, aided slightly, perhaps, by the natural elasticity of the lung-tissue, is mainly effected by the united forced efforts of the thoracic and abdominal muscles compressing the yielding bony cage.

The action of the ribs, both in sneezing and coughing, is made very clear by a glance at their respective stethographic tracings, which are here appended; and tracings of the course of the anterior ends of the ribs, in the acts of nose-blowing and yawning, are also given.

In one set of experiments, after an inspiration and sudden closure of the nose and mouth, the air was allowed to escape rapidly, as in the action of nose-blowing. The results were as shown below (Fig. 20); curves *a*, *b*, and *c* being the course taken by the third rib whilst the nose was blown once, and curve *d* when it was blown twice, during one expiratory effort.

In *nose-blowing*, the record was taken in order to ascertain the effect of suddenly closing the air-passages at the end of a deep inspiration. It will be seen that, in every instance, there is a slight forward bulging of the end of the rib; owing probably to the pressure of the compressed air in the chest, followed by the simple descent of the lever without any indrawing at the end of expiration.

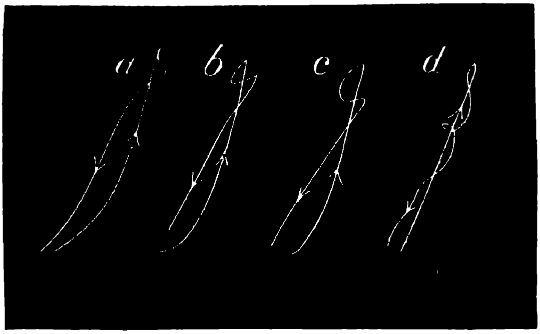

FIG. 20.—Action of the ribs in nose-blowing.

A series of short, voluntary coughs was then made, with a general result such as may be exemplified by the four tracings here given (Fig. 21).

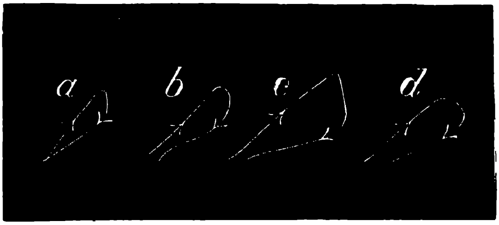

FIG. 21.—Single acts of coughing

In each case the tracings were taken from the ends of third ribs.

In *yawning*, the irregularity of the up-stroke shows the wavering, half-gasping nature of the inspiratory effort; and there is no anterior bulging at the end of the up-stroke, but an immediate descent of the rib-lever (Fig. 22).

In *sneezing* there is first the almost rectilinear track of quick inspiration, and afterwards the downward drop of the rib, followed by a very strong indrawing of its end. There is no stoppage at the beginning of expiration, and no bulging of the chest-wall (Fig. 23).

In *coughing* there is apparently a combination of the efforts made during nose-blowing and sneezing. But there are at least two distinct ways of coughing—the first, in which closure of the glottis takes place immediately after inspiration (as in Fig. 21); the second (Fig. 24, *a*), in which the act of violent inspiration is commenced, and the glottis is not closed until the rib has made some progress in its descent. A stoppage in the exit of the air then occurs, the rib is first bulged forward,

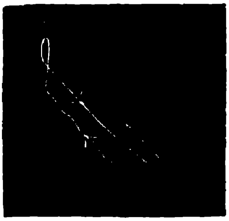

Fig. 22.—"A yawn."

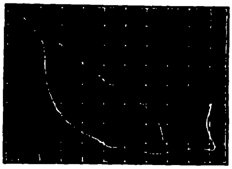

Fig. 23.—"A sneeze."

and then, on the opening of the glottis, is drawn inwards with a violent expulsive effort. Again, it seems probable that in some cases there is no complete closure of the glottis, but that the air is driven forcibly through its narrow aperture. In this case there is no forward push of the rib (Fig. 24, *b*).

In the acts of compound coughing (Figs. 25 to 27) the glottis is closed several times during one expiratory effort. Yet the tracings of these complicated acts present a strong family resemblance. In most of them, as we have seen, there is a slight forward bulging of the rib at the end of the inspiratory act, amounting in Figs. 25 and 27 to about 0·05 in.

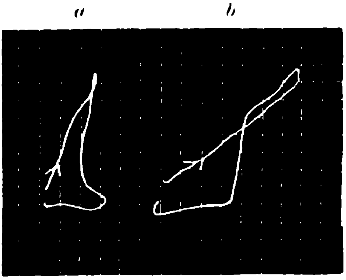

Fig. 24.—Varieties of cough.

This appearance must probably be attributed to the expulsive efforts of the respiratory muscles, which compress the air in the chest and so force the ribs outwards. No sooner, however, is the air released from the windpipe, than there is at once a downward fall of the rib, for a space of from 0·2 to 0·5 in. with a barely perceptible inward inclination; then comes a sudden change in its course, and it is drawn almost horizontally inwards, until it is caught by the second sudden stoppage of the glottis.

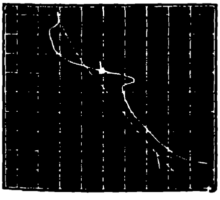

Fig. 25.—Double cough.

At the beginning of a second act of coughing the motion of the rib is either arrested for the moment, as in Fig. 25, or it is pushed forwards and even upwards by the compressed air in the chest (Figs. 26 and 27); and then, when it is again released, there is usually a still further bulging forward, together with a downward drop; and finally there is the almost horizontal indrawing of the rib. It is interesting to note that the extent of the forward bulging is greater the lower the rib gets in its descent —as if the rib yielded to the pressure within the chest more easily when in the position of partial expiration than in that of full inspiration. This is seen in Figs. 24 *a* and 27.

The following tracings of the movements of the third ribs and of a cough in a case of chronic phthisis show the strong contrast between these movements and those already given in a healthy person (Figs. 28 and 29).[1]

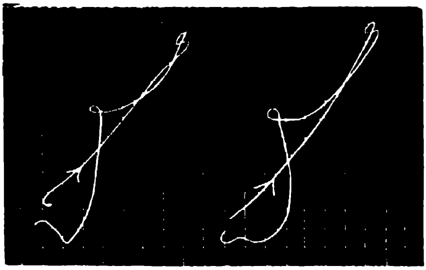

FIG. 26.—Double cough.

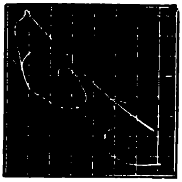

FIG. 27.—Three acts of coughing.

The effects of coughing in different diseases.—In the early stages of *acute bronchitis*, the expiratory inbending of the ribs adds to the force with which the air is driven over the dry and inflamed surfaces of the lining membrane of the trachea and bronchi, and increases the pain. After the first twenty-four hours, when proliferation and desquamation of the epithelium begin, the cough, if not too violent, may even exert a beneficial influence, assisting in the removal of suppurative or decomposing secretions, and thus tending to prevent the destruction of tissues; this action is all the more important as in this disease ciliary action is early arrested.

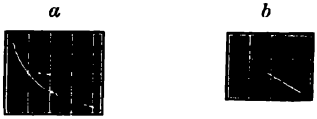

FIG. 28.—Chronic phthisis. Movements of third ribs.

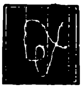

FIG. 29.—Cough in chronic phthisis.

These latter remarks apply also to *chronic bronchitis*; but the temporary relief afforded by coughing is then often followed by injury to the bronchial wall, especially when atrophic and indurative changes have taken place, and the bronchial wall becomes a mere fibroid tissue.[2]

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[1] This is not the place to discuss the possible causes of the expiratory shortening of the chord-lengths of the ribs in forced expiratory efforts; I believe that it is accomplished by the combined action of both sets of intercostal muscles, acting in concert with the abdominal muscles, the intercostals acting like the compressors of the pharynx, or the two oblique muscles of the abdominal walls. Suffice it to point out that its effect is to intensify all the consequences of ordinary expiratory efforts. It is true that, in disease, the respiratory function is greatly weakened (see "Prognosis in Lung-disease"), but all the more on this account is it necessary to take account of any additional aid to the expulsive forces engaged in the acts of forced breathing or coughing, and to note the effect of the compression that is thus exerted upon the thoracic contents.

[2] Dr. Auld remarks (*Pathology of Bronchial Affections and Pneumonia*, London, 1891, p. 56) "that in chronic bronchitis also, the retention of decomposing secretions has a considerable influence over the changes." These are removed by coughing.

In *pneumonia*, cough is often not a prominent feature; when it is, it may do but little harm to the inflamed portion of lung. In this disease, it is most likely that the inflammation is precipitated upon the organ by some specific irritant, which causes the general symptoms of a fever, and has its own special site of local manifestation. The consolidated lung cannot be compressed, but it may be injured by the respiratory efforts. Moreover, in most cases, the bronchial epithelium is uninjured in the non-inflamed parts of the lung, and hence there is the less need of cough to deal with the stained muco-pus.

During the stage of resolution the cough may be beneficial by clearing the blocked-up bronchioles; and in subsequent stages, if not too violent, it may do more good than harm, even when resolution is imperfect, and degenerative changes are taking place.

In the early stages of *pleurisy* the painful, irritable cough can scarcely do anything but harm, since it tends greatly to increase the friction between the folds of pleura. Usually, when effusion has taken place, cough diminishes in intensity.

In *fibroid* or *cirrhotic disease*, and in *broncho-pneumonia*, the cough, if at all pronounced, which is unusual, is likely to be harmful in proportion to the disorganisation of the lung-tissue, and to the tearing action that it may have upon bands of indurated interstitial material.

In *phthisis* the cough may be chiefly of laryngeal origin; in this case it is purely distressing, and can do little or no good; but when the patient coughs, as often he does voluntarily to relieve the lungs of secretion, the action is remedial and cannot be checked without harm.

It is in the production of *emphysema* and *bronchiectasis* that cough plays the most pernicious part. Whether inspiratory or expiratory forces be chiefly concerned in the result is still in dispute; but there can be no doubt as to the powerful influence of cough in the permanent dilatation of the alveolar walls and air-vesicles. An admirable account of this result of cough is given by Sir W. Jenner in his classical article on "Emphysema" in Reynolds' *System of Medicine* (13). He further points out that, as the disease progresses, the relative positions of the lungs and the chest walls are being continually shifted, and that fresh portions of the lungs are thus being continually brought opposite to ribs and to intercostal spaces respectively; thus, ultimately, the air-vesicles of the whole lung may be over-distended. I would venture to point out, however, that as the ribs are raised there is less and less power in the expiratory efforts. The movements are diminished in all the dimensions, and the progress of the disease may often be measured by the extent to which this impairment of motion has gone. It is very striking in this regard to compare the movements of a healthy chest with that of an emphysematous person; the following figures (30 and 31) give a graphical representation of these movements:—

In consequence of this loss of respiratory movement of the thorax, both in inspiration and expiration, the chest walls can only assist in producing the earlier stages of the disease: as it advances, the chief influence in determining the evil effects of cough must be that of the diaphragm and of the abdominal muscles.

Ultimately, owing to the extreme distension of the lungs, even the diaphragm is pressed downwards and rendered almost useless: under these circumstances the further progress of the disease would seem to be impossible. But, both at this stage and at an earlier period, the distensive force of the dilated lung itself comes into play. The air, either partially or entirely shut up by thickened secretions within the distended alveolæ and air-vesicles, is compressed with constant and elastic force by the elevated ribs, and under this pneumatic pressure the weakened walls of those portions of the lung that are unsupported by bony or cartilaginous structures are steadily dilated still further. The importance of this persistent pneumatic pressure, after a certain degree of distension has been attained, must not be lost sight of in estimating the morbid influence of cough.

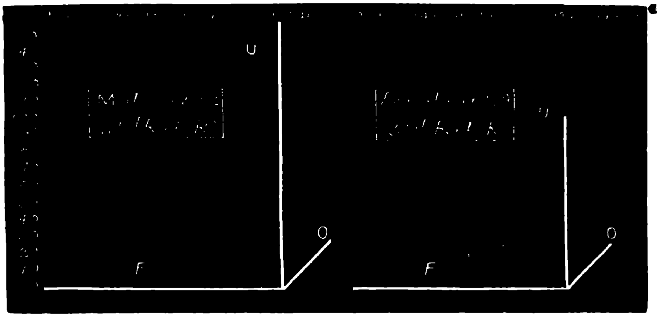

Fig. 30.—Relative dimensions of healthy movements.

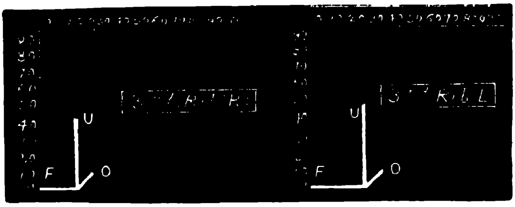

Fig. 31.—Dimensions of movements in a case of advanced emphysema.

In *bronchiectasis* the damage done to the air-tubes may also be either inspiratory, from a stretching of the walls of the bronchi by fibrous tissue bands in cirrhotic lungs—the pleuritic adhesions acting as a fixed point —or expiratory, and due to pressure of the air, as a cough may act upon bronchi whose walls have been damaged by inflammatory or atrophic changes. In either case, the hurtful effect of the cough may be intensified by any inbending power in the rib-levers, as such indrawing by pneumatic pressure may reduce the calibre of some portions of the bronchial tube, and dilate others. Dr. Auld (*op. cit.*) thinks that too much stress has been laid on the thoracic changes and on the air-pressure, and too little on the changes in the pulmonary tissue. Most true bronchiectases are of the moniliform type, and the pressure of air is inadequate to account for this. Where portions of the lung are collapsed and atrophous, the bronchial wall will expand to fill up the vacancy.

The more remote consequences of cough.—When cough is at all violent in character, its remote results are mainly due, first, to pressure upon the heart and great vessels, and next, to changes in the lungs causing an impediment to the flow of blood through the pulmonary capillaries. Owing to the powerful action of the expiratory muscles, a paroxysm of coughing causes a rise of arterial pressure; and this, together with the direct pressure of the thorax upon the vessels, greatly impedes the entrance of the blood from the systemic veins into the heart. Hence, in convulsive coughing, such as we observe in whooping-cough and some forms of bronchial irritation, we often see enormously swollen jugular and facial veins, and, not infrequently, hæmorrhages from the nose, or ecchymoses into the conjunctiva; and, although these effects are usually temporary, if they are frequent, they may end in permanent mischief.

Cough also influences the chemistry of respiration; in his Croonian Lectures for 1895, Dr. Marcet has shown that in coughing, as in asphyxia, there is a tendency to a want of oxygen and to a distinct excess of carbonic acid in the blood. Thus, he says, "In coughing a long breath is taken, which is exactly like a deep or forced inspiration, in which, as I have shown, a certain amount of carbonic acid is produced for work done—the oxygen being derived from that pre-existing in the contracting muscles, while a larger volume is displaced from the blood by a purely physical process; but, though forced breathing is attended with but comparatively little work in coughing, the respiration is laboured, the muscles having to strain against the closure of the larynx, and forcibly expel the air from the lungs. This results in the production of an excess of carbonic acid; hence, at the end of the expiration, there is an increased amount of carbonic acid in the circulation. After the forced expiration of coughing, a deep breath is taken to supply the blood with a fresh quantity of oxygen, and to rid it of the excess of carbonic acid produced, and this process goes on till the fit of coughing comes to an end, then deep inspiration and expiration follow till the blood is again perfectly aired, and the carbonic acid in excess is completely eliminated." The frequent repetition of this concentration of carbonic acid in the blood is sure, sooner or later, to end in damage to the tissues and to the heart.

In the heart, as a consequence of incessant cough, the first changes are usually hypertrophy and dilatation of the right auricle and ventricle; and the second is engorgement of the whole venous system. The systemic circulation is next affected, and organic changes in the left heart ensue. Sooner or later, in consequence of these impediments to the circulation of the blood, changes follow in other organs, such as the liver and kidney. The liver is first enlarged from simple congestion, then its tissues undergo alteration, and finally granular atrophy is the result. The kidneys suffer congestion and undergo structural change, and albuminuria is not infrequently the ultimate result. The connective tissue throughout the body also suffers from the mechanical obstruction to the blood-flow, and anasarca and other consequences supervene.

In brief, the results of coughing fits, frequently repeated, or long-continued, in debilitated persons with weakened and unhealthy tissues, are, first, changes in the lungs themselves, next in the heart, and afterwards in the system generally.

Many of these consequences of the "explosive" respiratory actions are also to be observed in the course of protracted dyspnœa, and the mechanism of this action must next be considered.

Dyspnœa, or difficulty of breathing, ensues to some degree whenever the natural interchange of gases fails, from any cause, to take place to the satisfaction of the needs of the body.

(1) When the air is deficient in oxygen, or overcharged with carbonic acid, or otherwise rendered partially or entirely irrespirable; as in rare faction of the air in mountain or balloon ascents, in poisoning by carbonic acid or other gases [*vide* art. "Mountain Sickness," vol. iii. p. 458].

(2) When the air-passages are not sufficiently pervious, or the respiratory movements are inadequate from any cause; as in the case of such mechanical and physiological impediments as new growths, or spasmodic closures of the air-inlets or air-tubes; or of defects in the action of the bones and muscles of the thoracic wall, as in paralyses of the respiratory muscles, meteorism, or abdominal tumours.

(3) When by extensive disease or injury the lung-tissues are so damaged, or otherwise so deficient, as not to expose a sufficient surface to the air.

(4) When the blood, either from cardiac or pulmonary defect, cannot flow freely through the capillaries of the lungs; or when these vessels are thickened and rendered unfit for the passage of gases across their walls, as in emphysema and inflammatory deposits.

(5) Finally, when the respiratory centre in the bulb is irritated, as in fevers; or when the vagi are so affected by disease as to convey undue stimulus to the medulla. In any of these many contingencies the rate of breathing, or the labour of accomplishing this act, will be increased.

In a word, the current need of the body must be under-supplied before dyspnœa can take place. The absence of this condition may account for the absence of serious symptoms even when grave injury has been inflicted upon the respiratory apparatus.

Degrees of dyspnœa in different diseases.—Dyspnœa may not arise even after considerable tracts of lung-tissue have been rendered useless.

In the true sense of the word, it is seldom a prominent symptom in the course of diseases of the respiratory organs, with the exception of asthma, emphysema, pneumothorax, and certain thoracic tumours; and yet it is in most cases the immediate cause of death.

It is interesting in this respect to compare cardiac with pulmonary diseases. In the former, the difficulty of breathing, as a rule, is constantly present, more or less, even when the patient is confined to bed; in most lung diseases it only appears on exertion, and in the latter indeed it is rarely true dyspnœa, except in those cases of obstruction of the air-passages, which are liable to be confounded with heart disease, when the breathing is laboured and retarded in frequency.

The respiratory movements are often rapid and shallow in *pneumonia* and *tubercular disease;* but the patient is scarcely conscious of effort. The air enters easily into the pervious portions of the lungs, but it has to be carried thither more frequently.

In advanced cases of *pulmonary tubercle* in which considerable destruction of lung substance has taken place, it is often remarkable how tranquil the breathing remains unless when harassed by cough. It is only upon the supervention of pneumothorax, or some other accident, by which large tracts of lung-tissue are suddenly made useless, that actual difficulty of breathing comes on. Even the onset of *acute tuberculosis* is unattended by true dyspnœa, quickened respiration alone showing the gravity of the case.

Similar remarks apply to most of the acute inflammatory diseases of the lungs, but towards the close of a fatal attack true dyspnœa generally supervenes, owing to the presence of one or more of the conditions already mentioned.

In the following disorders it may also be present throughout a large part of the illness. Thus, in *acute bronchitis* the act of breathing is usually laboured, and there is a sense of tightness and oppression about the chest. In severe cases of *capillary bronchitis* also, especially in children, the dyspnœa may be extreme, and may amount to paroxysmal or constant orthopnœa with cyanosis and venous congestion; and, finally, asphyxia may set in more or less rapidly. In *pulmonary embolism* and *thrombosis*, in *collapse of the lungs* and in *pneumothorax* the suddenness of the accident and the rapid cutting off of the supply of air to the blood usually cause extreme dyspnœa, which often ends in general collapse and death. In pneumothorax the full extent of the dyspnœa is conditioned by the presence or absence of pleuritic adhesions, or by their position. In some cases of empyæma both pleural cavities have been opened and drained; and yet the lungs have expanded sufficiently for the aeration of the blood, and even without much dyspnœa following. In these cases pleuritic adhesions must have been present.

But, apart from stenosis of the air-passages and sudden accidental loss of breathing power, it is in *advanced emphysema* that the most visible signs of dyspnœa are apt to appear. The constant position of the ribs in emphysema is that of full inspiration; and hence all the voluntary muscles are continually in play. In this disease, therefore, it is not unusual to find the patient, during a paroxysm of coughing, sitting up in bed or in an arm-chair with all the signs of orthopnœa; the lips and hands blue, the face livid, the eyes protruding, the jugular veins distended, the body bathed in cold, clammy perspiration. In many cases the signs of venous congestion and of more or less cyanosis remain permanent, and the dyspnœa is apparent even during rest.

Again, in asthma and in blockage of the air-passages from any cause, dyspnœa may be extreme for a time. But in asthma, although inspiration be forcible, even to the extent of causing indrawing of the epigastrium and of the lower ribs, it is not often much impeded. Expiration, on the other hand, "presents the picture of a most laborious and tormenting, and, at the same time, fruitless struggle" (Bamberger). All the expiratory muscles, indeed most of the muscles of the body, are brought into play, and sometimes the urine and fæces escape involuntarily during the attack; yet even then sufficient power to empty the lungs may not be obtained. The resulting dyspnœa is usually extreme, the patient sits up or stands, leaning upon his arms and holding on with his hands in order to secure a purchase for the auxiliary muscles of expiration; the alæ nasi are agitated, there is intense anxiety, and more or less venous congestion and cyanosis of the face. All this is due to the expiratory efforts, and, if the attacks recur at all frequently, often leads to serious damage to the lungs and circulatory system. Dr. Marcet has suggested that an attack of asthma may sometimes be precipitated by the "momentary want of air produced by a bad fit of coughing"; asphyxia being occasionally productive of other forms of spasm.

The mechanism of an attack of true spasmodic asthma is, in fact, an irritation of some part of the reflex arc controlling the circular muscular fibres surrounding the bronchial tubes; and it is well known that the specific irritation may arise from many points in the vascular bronchial mucous membrane; from the stomach, heart and kidneys, or even perhaps from a gouty condition of the blood.

Dr. Foxwell has also suggested that in asthma there is "sudden peripheral tension" (spasm) of the pulmonary arterioles, and consequent pulmonary anæmia (8).

On the other hand, in *spasms of the glottis*, in *paralysis* of the *posterior crico-arytenoid muscles* of the larynx, in *croup*, and in *plastic bronchitis*, the dyspnœa is chiefly inspiratory, as in other modes of blockage of the upper air-passages. In these cases, as the patient cannot introduce the necessary quantity of air into the lungs without severe and almost convulsive efforts, there is always, during the attempts at inspiration, considerable retraction of the epigastrium, and of the yielding portions of the thorax; the lower ribs are drawn in; the intercostal spaces and the supraclavicular fossæ are deepened. The dyspnœa in these cases is often as pronounced and as severe as in cases of asthma, and leads to the same serious consequences; but it is more likely to lead to atelectasis, and to some form of bronchiectasis, than to emphysema. In *pleurisy* the shortness of breathing is mainly voluntary; it varies with the pain and the extent of the effusion, and if effusion take place rapidly it may even cause fatal asphyxia.

Effects of dyspnœa.—Rosenthal has proved by experiment that dyspnœa and asphyxia are mainly due to the deprivation of oxygen, and not to the accumulation of carbonic acid; that diminution of oxygen in the air breathed does produce the phenomena of dyspnœa, and that excess of carbonic acid does not. But at the same time there can be little doubt that the CO_2 has an important influence; CO_2 certainly, as we have seen, is the natural stimulant of the respiratory centre. It also excites the vaso-motor centre, and thus leads to rise in the blood-pressure, but as it paralyses the vaso-constrictor influence the blood-pressure soon falls. In this way it concurs with defect of oxygen in producing the phenomena of asphyxia.

The immediate result of deficient oxygenation of the blood is that the respiration is quickened and becomes deeper; and as the venosity of the blood progresses so do the respiratory movements increase, both in force and frequency, all the auxiliary muscles being brought into play. Very soon, however, the expiratory movements become more pronounced than the inspiratory, and finally pass into expiratory convulsions. Professor Burdon Sanderson thus explains these phenomena:—"One of the effects of diminishing the proportion of oxygen in the circulating blood is to excite the vaso-motor centre, and thus determine general contraction of the small arteries. The immediate consequence of this contraction is to fill the venous system, in the production of which result the contraction of the expiratory muscles of the trunk and extremities powerfully co-operates. The heart, being abundantly supplied with blood, fills rapidly during diastole and contracts vigorously, in consequence of which, and of the increased resistance in front, the arterial pressure rises. This last effect is, however, temporary; the diastolic intervals being lengthened by the excitation of the inhibitory nervous system, and the heart itself weakened by defect of oxygen, the organ soon passes into a state of diastolic dilatation. Its contractions become more and more ineffectual till they finally cease, leaving the arteries empty, the veins distended, its own cavities relaxed and full of blood."

As the absorption of oxygen by the blood is to some extent influenced by the pressure, it is evident that we have, in inspiratory dyspnœa, a double impediment to the due aeration of this fluid; for the air is prevented from reaching the air-cells and the inspiratory efforts diminish the pressure within them. The symptoms in these cases should, therefore, be the more urgent, and I think that experience teaches us that this is the case. But the effect of dyspnœa upon the circulation soon equalises the results of all forms of difficulty of breathing, and hence we get very similar effects from dyspnœa, whether this primarily arise from the heart or from affections of the lungs.

It is possible that these observations may to some extent serve to explain the various degrees of intensity of dyspnœa in diseases of the lungs. In many of these affections the heart's functions are unimpaired, and hence the blood is driven evenly through such portions of the lungs as are pervious and to a great extent performing their natural functions.[1]

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[1] Cohnheim (3) quotes some experiments of Lictheim to show that a quarter the normal united sectional area is sufficient to allow the normal amount of blood to pass through the

With a certain increase in the rate of breathing, therefore, it is possible for the blood to be aerated sufficiently for the very moderate amount of exertion usually made by these sufferers. Such conditions obtain, for instance, in phthisis, in many cases of pneumonia and bronchitis, and in one-sided pleurisy.

Compensatory actions in dyspnœa.—There is also, in most of these disorders, a natural tendency towards compensation. The quickened breathing does more than bring increased supplies of oxygen to the air-vesicles. The increased supply of air would be of but little use unless sufficient blood were flowing through the capillaries of the lungs to fill the left auricle. But it is well known that even the ordinary movements of respiration materially assist the work of the circulation; much more then, in disease, will the quickened and forced efforts at breathing augment the velocity of the pulmonary circulation, and cause a larger surface of blood to be exposed to the air.

In his Croonian Lectures for 1895, Dr. Marcet shows that simple volition greatly increases the mechanical power of the muscles of the body; and he suggests that perhaps, in forced breathing, there is really an excess of oxygen absorbed, which is taken up by the brain centres of forced breathing, and gives "volition" the power of doing so much additional muscular work through increased respiration.

This hypothesis was submitted to experiment; and from the results obtained it "appears that, whenever volition is applied towards any form of exercise, there is an absorption of oxygen in the cerebral centres concerned in the phenomenon; and apparently with an excess of oxygen absorbed, more work can be done than if the excess be wanting." Here then we have at least two more forms of almost automatic compensation.

In long-continued cases, also, this compensatory action of dyspnœa is presently assisted by an increase in the power of the heart. If the nourishment of the general system, and with it of the heart, be not interfered with, its increase of work will gradually lead to increase of power and to increase of substance; in other words, to hypertrophy of the organ. In spite, therefore, of a certain loss of permeable substance of the lung, and a consequent smaller vascular area, the blood-stream may be forced more rapidly along the channels that remain, and the necessary degree of aeration may be accomplished.

Unfortunately these means of compensation are not always adequate. The balance of the pulmonary circulation with respiration is in a position of unstable equilibrium, and is liable, at any moment, to be upset by such causes as a slight cold, some little over-exertion, and so on. Patients may indeed discover that it is necessary to restrict their movements, and to alter the quantity and quality of their food; but, if life is to be carried on, they cannot reduce the metabolism of the tissues beyond a certain point. Sooner or later a greater degree of dyspnœa is sure to occur; nutrition becomes impaired, the heart loses power, the structural

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lungs. "This, however, is the lowest limit, beyond which the power of compensation fails" (*Lancet*, Feb. 23, 1895).

elements of the blood are affected, and either anæmia or cyanosis makes its appearance.

It must not be forgotten, also, that when, as we have seen, dyspnœa raises the general arterial blood-pressure throughout the body, the coronary circulation is not likely to escape its influence; hence the nutrition of the heart itself is carried on under difficulties, and is liable to fail at a critical moment.

The cyanotic condition.—One of the most frequent results of dyspnœa of a certain degree of severity is carbonisation of the blood, or the cyanotic state; (so called, probably, on account of its resemblance to the true cyanosis, the morbus cæruleus of the old writers, caused by the intercommunication of the right and left sides of the heart).

In respiratory diseases, characterised by a sufficient degree of dyspnœa, the symptom is due both to a deficiency of oxygen and an accumulation of carbonic acid in the circulating fluid, to an extent, in some cases, of a more than venous condition of the blood.

In ordinary venous blood, according to Stroganow (20), there is nearly 19 per cent of oxygen and from 6 to 9 per cent of carbonic acid; but in the blood of asphyxia the oxygen may entirely disappear, and the carbonic acid may rise to about 50 per cent.

It is certain, also, that in most cases of cyanosis there is an excess in the number of blood corpuscles. This has been observed by Toeniessen, Carmichael, Gibson, and others, and is ascribed by Gibson to an attempt at compensation. "In venous stasis, the corpuscles," he says, "are insufficiently oxygenated, they cannot perform such an active part as oxygen-carriers, and they cannot yield so much oxygen to the tissues. It must further be remarked that in cyanosis there is less metabolism in the tissues, and therefore less waste produced. In a word, the functions of the corpuscles being lessened, the wear and tear which they undergo is reduced, and the duration of their individual existence increased. The number of the corpuscles must in this way be proportionately augmented, and this must lead to the numerical increase, as well as to the high percentage of hæmoglobin" (9).

It seems certain that the oxygen in the blood is in a state of loose chemical combination with the hæmoglobin, and that the blood corpuscles can take up a sufficient supply of oxygen under circumstances of both low and high pressure of the atmosphere. It is thus difficult to exhaust the store of oxygen in the capillaries.

It has been shown by Muller that blood outside the body may be completely saturated with oxygen in atmospheric air of only 75 mm. of pressure; but at the temperature of the body decomposition of the hæmoglobin begins at a higher pressure.

Fraenkel and Geppart showed that it is not until the atmospheric pressure sinks below 300 mm. that a considerable decrease in the oxygen of blood takes place.

It is probably owing to these facts that on ascending high mountains dyspnœa is not observed until the mercurial barometer marks a pressure of less than 400 mm., and that Mr. Whymper in the Andes, and Sir Martin Conway in the Himalayas, were able to move in altitudes over 20,000 ft. (*vide* art. "Mountain Sickness," vol. iii.).

Drs. Haldane and Lorrain Smith also found in their experiments that cyanosis was not produced until the oxygen inspired fell below 9 per cent; and in one instance the air was breathed until the oxygen was reduced to 6 to 7 per cent. They remark that the tension of oxygen then found corresponds to that obtained by rising to a height of about 29,000 feet.

The occurrence of cyanosis may be due, then, either to an insufficient supply of air to the blood, or to a defective exposure of the blood in the capillaries to the air in the alveoli. It may consequently arise from deficient action either of the lungs or of the circulatory system. In the former case it may arise from stoppages in the air-passages, defective muscular power, and injuries to the lung-structures, or from destruction of or defects in the pulmonary blood-vessels; in disorders of the circulation it may come from imperfect propulsion of the blood through the pulmonary arteries, as in dilatation of the right heart or embolism or œdema of the lungs, or from backing up of the blood-stream going to the left heart, as in mitral stenosis.

From whatever cause it is impending, however, like dyspnœa, it may be staved off for a time, except in the case of complete occlusion of the air-passages, (*a*) by the respiratory efforts of dyspnœa, or (*b*) by limiting the demand of the body for oxygen. Dyspnœic efforts tend not only to increase the supply of air in the lungs, but also to increase the suction power of the thorax, and thus improve the pulmonary circulation. The production of carbonic acid and the need for oxygen may be diminished, and often are so diminished, in these cases, by reducing the muscular work as far as possible, and by regulation of the diet.

A third mode of resisting the tendency to cyanosis, and also to dyspnœa, is to augment the power of the right ventricle. By means of hypertrophy of the heart, the system gains the advantage of sending the blood more rapidly through the capillaries of the lungs, and exposes the necessary amount of blood to the air. It is marvellous for how long a period the existence of an extreme degree of mitral stenosis may thus be overcome.

The difference in the tolerance by the system of cyanosis originating in heart and lung troubles respectively may possibly be explained by these facts. I have often been struck by the long endurance of the cyanotic condition in cases of mitral stenosis, years passing with more or less blueness of the lips and extremities; but in advanced lung disease the onset of permanent cyanosis usually takes place but a short time before the end of life. The heart, in its diseased conditions, usually has the advantage of a very gradual onset of the symptom, and of being able to find unimpaired tissues in the lungs and an unlimited supply of pure air; but in lung diseases not only are these tissues in a more or less damaged condition, but the heart itself has also undergone some impairment of its power, and thus dyspnœa and cyanosis frequently come on very rapidly.

It is important to observe, however, that there may be no marked cyanosis even in very advanced disablement of the respiratory function, as, for instance, in the advanced stages of phthisis. In these cases, the hectic fever and the great emaciation lead to such a condition of anæmia that cyanosis cannot show itself. The blood corpuscles are too few in number to display either their red or their bluish tints, and extreme pallor is the only sign visible; moreover, there is little or no venous congestion, for the right heart easily sends on the scanty blood-current received from the general system.

In these and in other cases, therefore, there may be none of the usual evidences of asphyxia, dyspnœa, convulsions, dilated pupils, or other signs of irritation of the vaso-motor and vagus centres.

The muscular weakness may be so great that there is no response to the nervous impulses; or the brain, in the absence of sufficient oxygen to carry on its functions, may lose its irritability, and the respiratory centre cease to respond to the stimulus of over-abundant carbonic acid in the venous blood. Under such circumstances, as Cohnheim points out (5), "there is no extraordinary increase of dyspnœa and no convulsions; similarly the exophthalmos and the dilated pupils are absent, as well as the evidences of irritation of the nervous centres. Rather the pulse of such patients is usually small and easily compressible, very frequent and sometimes irregular; the pupils are normal or even contracted, and all the bodily movements feeble and languid.

"Instead of the cyanosis, which it is easy to see will be more apparent the more full-blooded and vigorous the individual, the face, skin, and visible mucous membranes of such patients take on a bluish gray, dull, almost leaden hue; the temperature is low, and the skin feels cool to the touch; for not only do the movements, but all the other functions gradually become paralysed: the patients grow markedly apathetic, or even somnolent, are unaware of all that goes on around them, and unconscious of their own need for air."

I have hitherto attributed the symptoms of asphyxia to absence of oxygen and superabundance of carbonic acid; but it is by no means certain that other poisonous materials are not present in the blood, which either themselves affect the respiratory centre, or intensify the influence of deficient aeration of the blood.

Thus Zuntz, and Lehmann, and F. L. Smith point out the influence of the products of muscular metabolism produced during exercise, and Jacquet shows that lactic acid acts as a direct excitant to the respiratory centre of the rabbit.

Dr. V. Harley shows that after the intravenous injection of sugar there is a marked decrease both of carbonic acid and oxygen in the blood; but the resulting coma and convulsions were not due to this cause, for the oxygen increased and the carbonic acid remained low before their onset.

It has long been known that a certain amount of organic matter is given off in the breath, and various attempts, especially by Tiedeman, Valentin, and Angus Smith, have been made to determine its nature and quantity. I have myself made a number of analyses of the aqueous vapour of human breath condensed by means of freezing mixtures, and have ascertained that, although remarkably constant in health, it varies greatly in different diseases. For our present purpose it may be sufficient to point out that the total quantity was much reduced in affections of the lungs, and that it was considerably increased in albuminuria and ozæna. There is still much difference of opinion as to the poisonous influence of this organic matter: Brown-Séquard and d'Arsonval may be cited on the affirmative side, and Haldane and Lorrain Smith recently on the negative. But to my mind it is at least important to remember that there is a possible danger from such retention in cases of defective respiratory power.

It is probable that, even in health, toxic substances are constantly excreted by the cells of the body, and that under certain circumstances they may accumulate in the system; as, for example, after over-exertion, disturbances of secretion or excretion, or as a result of diminished respiratory action. It is well known that malaise, headache, and other nervous symptoms often arise as a consequence of these conditions, and may with probability be ascribed to some toxic cause. Toxic alkaloids have been extracted from healthy bodies by Bouchard, Gautier, Coppola, Mosso, and Guareschi.

Dr. Farquharson gives a number of references to researches under pathological conditions in which toxic substances were extracted from the urine, intestines, and other parts, in various respiratory disorders, enteric fever, progressive paralysis, pernicious anæmia, uræmia, and so on. It is generally acknowledged, also, that many of the symptoms in diphtheria, phthisis, and tetanus are due to toxines derived from the specific bacteria. On the whole, we may say that a case has been made out for the assumption that some, at least, of the symptoms arising in the course of dyspnœa and asphyxia are produced by substances other than carbonic acid.

Cheyne-Stokes breathing.—Amongst the most interesting of the results of derangements of the pulmonary circulation must be placed the occurrence of "periodic," "tidal," or "Cheyne-Stokes" breathing.

Attempts to explain this occurrence have hitherto been without complete success. It seems to be acknowledged that one condition must be some lowering of the functional activity of the respiratory nervous mechanism; but this in itself cannot account for the regular periodicity of the phenomenon.

It is necessary, moreover, to bring within the scope of any satisfactory theory all the very diverse conditions under which it is known to occur—diseases of the heart, brain, and lungs, blood-poisoning of different kinds, the action of narcotics, insolation, nay, even the fact that it has been observed during apparently perfect health. It must also account for the concurrent symptoms that have been observed.

At present physiologists seem inclined to fall back upon the hypothesis that when, from any cause, the activity of the automatic centre is reduced, its functions have a tendency, common to all vital structures, to become periodic. Under ordinary conditions this tendency to periodicity in the respiratory movements is kept under control by the higher regulating centres; but when from any cause this influence is weakened, the natural rhythmical action of the centre comes into play. The phenomenon is thus brought into line with what is known as the Traube-Hering rhythm in the vaso-motor system; both rhythms are originated by medullary centres, and both are closely associated in their degree of frequency. Dr. Gibson (10), in his elaborate examination of all the hypotheses, sums up the matter thus:—"They are instances, among many others, of the common tendency towards 'pulsatile or rhythmic activity' manifested by all living matter."

There only remains a brief consideration of the rare but still possible occurrence of spasmodic breathing in the course of Bright's disease. Sir W. Roberts gives a case of this kind in his work on Urinary Diseases (p. 480). The accident is in truth more likely to arise in consequence of changes in the circulatory system, than from the supposed uræmic alterations in the composition of the blood itself. Yet it cannot be overlooked that the circulation of irritating refuse materials in the blood may lead to changes in the vessels of the lungs, as in other parts of the body. Moreover, it is at least significant that, in the analyses of the aqueous vapour from the lungs in cases of albuminuria, to which I have already referred, I found both more distinct traces of urea and a much larger quantity of oxidisable organic matter than in health, or in other diseases. These substances must interfere to some extent with the normal processes of oxidation (16).

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REFERENCES

1. AULD. *Path. of Bronchial Affections and Pneumonia.* Lond. 1891.—2. BERNARD, CLAUDE. *Revue des deux mondes,* Août 1865, Mars 1868—3. COHNHEIM. *Lect. on Gen. Path.* vol. iii. p. 1072. Syd. Soc.—4. *Ibid.* p. 1085.—5. *Ibid.* p. 1097.—6. FRAENKEL and GEPPART. *Ueber die Wirkungen der Verdunnten Luft.* 1883.—7. FARQUHARSON. *Ptomaines.* Bristol, 1892—8. FOXWELL. *Essays in Heart and Lung Disease.* London, 1895, pp 19, 20.—9. GAMGEE. *Phys. Chem.* vol. i. p. 15.—10. GIBSON. *Lancet,* Jan. 5, 1895, p. 25.—11. GIBSON, G. A. *Cheyne-Stokes Respiration.* Edin. 1892—12. HARLEY, V. *Proc. R. S.* No. 337.—13. JACQUET. *Arch. fur exp. Path. u. Pharm.* 1892, Bd. xxx. p. 11.—14. JENNER, Sir W. Reynolds' *System of Medicine,* 1871, vol. iii. p. 475.—15. MARCET. *Croonian Lectures,* 1895.—16. MARTIN. *Amer. Journ. Med. Sci.* March 1896.—17. RANSOME, A. *Proc. Lit. and Phil. Soc.*—18. *Idem. Stethometry,* p. 187.—19. ROSENTHAL. *Pfluger's Archiv,* vol. i. p. 94.—20. SANDERSON, BURDON. *Handbook,* p. 323.—21. SMITH, F. L. *Journ. of Phys.* 1890, vol. xi.—22. STROGANOW. *Pfluger's Archiv,* vol. xii. p. 22.

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THE TREATMENT OF ASPHYXIA

The treatment must necessarily depend upon the causes in each particular case; especially whether the symptoms of partial suffocation be due to mechanical obstruction of the upper air-passages, to immersion in water or irrespirable gases, or to some more deeply-seated affections. Cessation of the heart's action is a complete bar to any hope of resuscitation from asphyxia, however produced; but it has been clearly shown by Sir B. Brodie and others that in some cases, after the cessation of breathing, the heart may continue to act for two or even four minutes. Moreover, it is not always easy to ascertain the exact moment at which either of these actions ceases, for partially effective efforts to breathe may have been made for some time after apparent stoppage.

Death from drowning may, however, occur in spite of the continuance of the heart's beat, owing to the presence in the lungs of irremovable watery froth; or the gases causing asphyxia may be poisonous in their nature, and death may take place from shock or semi-paralysis.

We cannot, therefore, be quite sure when hope must be abandoned; and we are bound to use all the means of resuscitation, even though ten minutes or more may have elapsed since apparent death.

Before any special treatment can be adopted, the passage for the air to the lungs must be made clear; foreign bodies must be removed from the pharynx or larynx, preferably with the finger, after the mouth has been wrenched open, and any handy gag inserted between the teeth failing the finger, a blunt hook, such as a large button hook, or laryngeal forceps, or a probang, if available, may have to be used. If the air-passage is not speedily opened up, intubation of the larynx or, even tracheotomy may have to be performed on the spur of the moment. Similar means must also be used in cases of obstruction from other causes; such as occlusion by diphtheritic membranes, or tumours about the rima glottidis, or palsies of the abductors of the vocal cords.

When the air-passages are free, efforts at resuscitation must immediately begin: at first, we make simple pressure upon the thorax and abdomen simultaneously every two or three seconds, but if this do not speedily produce signs of air passing in and out of the lungs, one of the methods respectively known by the names of Marshall Hall, Sylvester, and Howard should be put in practice.

Marshall Hall's ready method simply consists in placing the body on its side, then rolling it over on the face, then on the opposite side, and on the back; repeating the process twelve or fifteen times in a minute. This plan has the advantage of not needing any assistant.

Sylvester's method.—"Place the patient on his back, on the floor, with a block or pillow under his shoulders, and raise the arms upwards above his head, by grasping them above the elbow, or better still, by seizing the anterior folds of the axillæ so as to raise also the clavicles; the upward pull must be continued firmly and steadily as long as there is any sound of air entering the chest. The head must be permitted to fall back over a block or cushion placed behind the neck, so as to open the larynx, or failing this, the tongue may need to be pulled sharply forwards by forceps or a noose of string, or by grasping it with a handkerchief.

"As soon as the sound produced by the entrance of air into the chest ceases, the arms should be brought down a little towards the front of the chest, and pressed down firmly and steadily against it for about one second after air is heard escaping. This operation is usually repeated every four seconds, but, in the case of poisonous vapours, such as those of chloroform, carbonic oxide or acid, it may need to be done more rapidly for a few minutes so as to quickly empty the lungs of the vapour."

Howard's method.—This method, in cases of drowning, has the advantages of facilitating at first the trickling away of watery fluids and the dislodgment of foreign bodies. Dr. Howard gives the following directions in the first instance:—"Position of the body: face downwards. A hard roll of clothing beneath the epigastrium, making that the highest point, the mouth the lowest. Forehead resting on fore-arm or wrist, keeping the mouth from the ground.

Position and action of operator: Place the left hand, well spread, upon the base of the thorax to the left of the spine; the right hand upon the spine, a little below the left, and over the lower part of the stomach. Throw upon them, with a forward motion, all the weight and force the age and sex of the patient will justify, ending this pressure of two or three seconds by a sharp push, which helps you back again into the upright position. Repeat this two or three times, according to the duration of the immersion, and then proceed to artificial respiration as follows:—

Position of patient: face upwards. A hard roll of clothing beneath the thorax, with the shoulders slightly declining over it. Head and neck bent back to the utmost. Hands on the top of the head. Strip clothing from waist and neck. Position of operator: kneel astride patient's hips; place your hands upon his chest, so that the ball of each thumb and little finger rest upon the inner margin of the free border of the costal cartilages, the tip of each thumb near or upon the xiphoid cartilage, the fingers dipping into the corresponding intercostal spaces. Fix your elbows firmly, making them one with your hips. Action of operator: pressing upwards and inwards towards the diaphragm, use your knees as a pivot, and throw your weight slowly forwards for two or three seconds, until your face almost touches that of your patient, ending with a sharp push which helps to jerk you back to your erect kneeling position. Rest three seconds; then repeat this movement as before, continuing it at the rate of seven to ten times a minute; taking the utmost care, on the occurrence of a natural gasp, gently to aid and deepen it into a longer breath until respiration becomes natural."

This method is said to keep open the passage through the larynx without the aid of an assistant, or any contrivance for the purpose. During the use of any of these methods the temperature of the body must be kept up by hot blankets and hot bottles; and if the means are at hand it may be well to try galvanising the phrenic nerve or the heart; but the attempt should only be a short one. An injection into the rectum of warm beef tea, with a little brandy, may also be administered. The extremities should be constantly rubbed with warm hands, but without exposing the patient.

The Royal Humane Society has published some excellent rules, embodying in the main Dr. Sylvester's method.

Mr. Francis' method.—The body having been laid on the back, with clothes loosened, and the mouth and nose wiped, two bystanders pass a narrow lever of any kind under the body at the level of the waist, and raise it until the tips of the fingers and the toes of the subject alone touch the ground; count fifteen rapidly; then lower the body flat to the ground, and press the elbows to the sides hard; count fifteen again; then raise the body again for the same length of time, and so on, alternately raising and lowering; the head, arms, and legs are to be allowed to dangle down quite freely when the body is raised.

Of course other aids for restoring the circulation are not to be neglected.

Mr. Francis thinks that the position of the body, when raised as described, mechanically puts upon the stretch all the muscles of inspiration, except the external intercostals; and that the position of the ribs, sternum, and clavicles allows their weight to aid considerably in the expansion of the thoracic cavity. The intestines and abdominal viscera also gravitate towards the pelvis, and must draw down the diaphragm.

Laborde's method of inducing respiration, by making rhythmical traction upon the tongue, is well worthy of trial, especially when the operator is alone. The method is fully discussed, and experiments quoted, by Dr. Edward Martin (*Amer. Journ. Med. Sci.* March 1896). The tongue is drawn forward during attempts at inspiration, and released for expiration, twelve to fifteen times in a minute. When more than one helper is present, the Sylvester movements must also be made, accompanied by the above-mentioned traction and relaxation of the tongue in inspiratory and expiratory movements respectively.

When the causes of asphyxia are more deeply seated, and arise from profound affections either of the lungs or heart, there is usually less need of that immediate action which I have just described. Yet there are cases, even in this class, in which life has been saved by the early recognition of the tendency to death, and by the prompt application of means for the restoration of the balance between circulation and respiration.

Thus in cases in which, owing to a failure in the natural functions of either heart or lungs, the right heart has become over-distended with blood, and cannot properly expel its contents, means of relieving this engorgement may be instantly called for. Even in these days of popular prejudice against blood-letting I have several times seen immediate relief given by prompt venesection, and life thus saved for considerable periods.

In less serious cases it may be possible to afford the necessary relief by other means directed towards the removal of the venous stasis; such measures are free dry, or even wet, cupping of the chest, back and front; the application of Junod's boot; the use of stimulating, hot fomentations; or, better still, of the hot-air bath; or the envelopment of the body in blankets wrung out of hot mustard and water, covered by a dry blanket and by waterproof sheeting—the "blanket bath."

Again, after some relaxation of the immediate distress has been obtained by such measures as these, there are few means that give such comfort as the regular use of a mercurial pill, on alternate nights, and the occasional administration of some hydragogue purgative, such as pulv. jalapæ co. or Carlsbad salts.

In some cases it will be necessary to tap the abdomen for ascitic fluid, in others to insert Southey's tubes into the feet or legs. To remove fluid effusions from one or both pleural cavities often gives striking relief. Again, in all cases of great difficulty of breathing much relief may be conferred by administering pure oxygen, such as may now always be obtained from Brin's Oxygen Company. It may be given, without danger, undiluted, by means of a Clover's inhaler, or of a simple rubber tube and mouthpiece; but in many instances it suffices to deliver a stream of the gas close to the mouth.

I have also found great benefit, when the lips and finger-tips are becoming cyanotic, in giving by the mouth from twenty to thirty drops of Richardson's ozonic ether. It should be given in pure water, and should not come in contact with any organic matter, as the ozone it contains is soon destroyed. It often brings back the ruddy hue to the face and hands, and has been a source of much comfort even to the dying.

It is scarcely necessary to add that, when occasion offers, all other means in our power should be brought into play to give increased power to the heart to expel its contents; such drugs, for instance, as digitalis, nux vomica, and quinine, strophanthus, Virginian cherry, and so forth. In all such cases diet and stimulants must be carefully regulated so as to spare the labour of the vital processes to the utmost.

A. Ransome.

PHYSICAL SIGNS OF THE DISEASES OF THE LUNGS AND HEART

PHYSICAL signs may be regarded as embracing every impression, made on our organs of sense, capable of giving information concerning the physical condition of the human body and its organs. It is only as the result of observation and experience that the value of the impression can be estimated and the conclusion rightly drawn; the inference must, however, always be clearly distinguished from the sign itself. It is chiefly by the correct observation of physical signs that it is in our power to obtain trustworthy knowledge of the state of the several organs of the body in respect of health or disease.

The impressions which the patient himself receives are in a certain sense to him physical signs. These, however, although valuable, for the most part, do not afford exact information, and when resulting from disease are generally called symptoms. Without physical signs, symptoms frequently tell us nothing of the nature or seat of a malady. Various instruments have been invented or employed which, like the thermometer or sphygmograph, add to the precision of our observations, like the ophthalmoscope or laryngoscope extend their range, or like the stethoscope or microscope increase their power. Sight, touch, smell, and hearing may each separately receive impressions from external objects, and from these impressions we are accustomed to draw conclusions as to the physical conditions of the objects concerned.

In the case of the internal organs of the body, unaided vision, so far as ordinary light is concerned, is limited to the observation of the effects produced by the internal movements on the surface of the body, or of the alterations of shape, movement, or appearance which may take place at the surface from altered internal conditions. The ophthalmoscope, the laryngoscope, and a variety of specula enable us to bring vision to bear on parts otherwise out of sight.

Touch may be employed to estimate the force and determine the position of the heart's beats, or to observe the frequency, regularity, and strength of the pulse, or to detect the presence of tumours in the abdomen or elsewhere, or the enlargement of any of the organs which are accessible to palpation. Sight, and even more certainly touch, will reveal the existence of pulsation in an abnormal place. The sense of touch is of great value also in determining whether a tumour is fluid or solid. Smell may assist in the recognition of such conditions as ozæna, gangrene of lung, bronchiectasis, diabetes mellitus or other diseases which are attended with a characteristic odour; but its uses are narrowly limited, because there are but few of the organs of the body and few diseased conditions which have a distinctive odour. Taste is the only sense which, for obvious reasons, cannot well be applied to practical use.

The physical signs, however, which specially concern us here are those which have to do with the vibrations of sound and the impressions made by them principally on the organs of hearing; although to a minor degree they affect the sense of touch also. The two great means of physical examination which we possess are known as auscultation and percussion. Auscultation simply means the listening to the sounds which are produced within the body. Percussion consists in striking a part of the body in a special way and listening to the sound thus produced.

The sounds observed in auscultation produced from within and the sounds of percussion produced from without are of the highest importance as physical signs.

In order to have a clear conception of the meaning of these physical signs which we are now about to consider, it is absolutely essential that certain acoustical principles should be enunciated and borne in mind. These principles are the laws which govern (I.) the production, and (II.) the conduction of sound; without these it is impossible to understand or properly to interpret the phenomena connected with auscultation and percussion.

I. **The production of sound.**—All sound depends upon vibrations, which vibrations must be conducted to the organ of hearing. Vibrations may occur primarily in solids, liquids, or gases; and they may be conducted from one to the other before ultimately reaching the ear.

Sounds in general may be roughly divided into two classes according as the vibrations which produce them are regular, continuous and periodic, or the reverse. The sounds produced by vibrations of the first class are called musical, those produced by the second class of vibrations non-musical sounds or noises. Noises are irregular, confused, and interrupted, and as a rule sound harsh to the ear, while musical sounds are more or less agreeable to it. In practice, however, it is difficult to draw a sharp distinction between a musical sound and a noise. Few musical sounds are entirely free from noise, and many noises have some musical quality. The special quality of a musical sound is what is known as *pitch*, which is determined by the frequency of the predominant vibrations per second. Very slight differences in pitch can be accurately distinguished by the trained ear. No sound which has pitch can be wholly unmusical. We refer to pitch when we say a sound is acute or grave, shrill or low, high or deep, sharp or flat. In addition to pitch, musical sounds possess three further properties: namely, (*a*) loudness or intensity, (*b*) duration, and (*c*) character, quality, or timbre. Of loudness and duration no explanation is required; we speak of sounds as being loud or feeble, short or prolonged. It is otherwise, however, with the property of character, quality, or timbre, which enables us to distinguish notes of the same pitch when sounded on different instruments, and causes us to characterise them on the one hand as rich, sweet, mellow, or full, or on the other hand as poor, harsh, nasal, or thin.

Some confusion has been introduced into medical literature by the use of the word *tone* in a sense different from the strictly scientific one it possesses in acoustics. It has been stated, for instance, that musical sounds possess loudness, duration, pitch, and tone, and that what distinguishes one percussion sound from another is the possession of tone. This is clearly making tone the equivalent of timbre. Now a tone in acoustics is a sound of a definite pitch and incapable of analysis into simpler sounds. All ordinary musical sounds are harmonious combinations of tones. Where the periods of vibration are as 1, 2, 3, 4, etc., the corresponding sounds combine agreeably. No pure tone can be said to have timbre. *Timbre* depends on the mode in which higher tones, which are called harmonics, are combined with the lowest or fundamental tone in a musical sound. A trained ear can recognise the individual tones which go to make up a note, as sounded by such instruments as the piano or violin.

The subject of musical tones is closely connected with the theory of what is known as resonance, another term which in medicine has unfortunately been used in quite an inaccurate sense. The acoustical theory of resonance has an important connection with some of the sounds met with in percussion and auscultation, and it is therefore necessary to enter into some little detail concerning it.

We have referred to the fact that sounds may be produced by the vibrations of circumscribed portions of a gas as well as by the vibrations of liquids or solids. An enclosed column or other mass of air can be made to vibrate with a definite period and produce a musical sound possessed of definite pitch. It will also possess the property of giving out such a sound when a sound of its own pitch reaches it from the external air. The term *resonance* is used to denote the reinforcement of sound, by an enclosed volume of air communicating with the external air, due to the synchronism which exists between the vibrating period of one of the tones which compose the sound and that of the volume of air. The instrument possessing the air-containing cavity is called a resonator. The disturbance of the air produced by a mere noise in the neighbourhood of a resonator may throw the air in its interior into vibrations and cause it to give out its own note.

The *resonators* devised by Helmholtz are hollow globes possessed of an ear-piece fitting into the external meatus at one pole, while at the opposite pole is a larger opening communicating with the external air. When the note which corresponds to this resonator is sounded it becomes enormously intensified. With a series of such resonators an ordinary musical sound can be analysed into its component parts, and the presence of a variety of simple tones may be discovered in what might itself be regarded as a simple sound.

A simple tone unaccompanied by harmonics is dull and uninteresting, and if of low pitch is destitute of penetrating quality.

When a body capable of vibrating is struck it will emit a sound; and conversely if it emit a sound it is able to vibrate. Capability of vibration shows that it is to some degree elastic. The sounds emitted by different bodies vary immensely, depending, as they do, on the nature of the substances, as well as on their size, shape, elasticity, and so forth.

In the case of membranes and strings a certain degree of tension is required before vibration, in such a way as to produce a musical sound, is possible.

Bodies with slight elasticity will vibrate little; they will produce but feeble sound, and that of a dull damped character without much of the musical element.

Bodies possessed of a fair amount of elasticity, on the other hand, will vibrate freely; they will produce a considerable volume of sound, and this with a good deal of the musical character. Lead has very little elasticity, and emits when struck a characteristic dull sound without any ring in it. Fleshy organs, like the liver, spleen, kidneys, heart, or consolidated or collapsed lung, are possessed of little elasticity and produce a dull dead sound when percussed. The air-containing lung is highly elastic, and when distended will vibrate freely when struck, producing a full rotund sound. Similarly, the membrane of the stomach or intestines, when distended by the gases in its interior, can vibrate freely. When the pleural cavity is filled with air the thoracic wall, which is highly elastic, can vibrate freely, and a full-toned sound is produced. When, on the other hand, the pleural cavity is filled with fluid, vibrations of the thoracic wall are damped at once, and a dull dead sound is the result.

Percussion.—Long use has rendered classical the terms *resonance* and *dulness* as applied to the sounds elicited on the one hand by percussion of a part of the body which can vibrate freely, as the chest wall over the lungs or a pneumothorax; and on the other by percussion of a part where the vibrations are damped, as the chest wall over a pleuritic effusion or consolidated lung.

The acoustical theory of resonance has led some authors to seek a similar explanation for the resonance just mentioned. Thus an attempt has been made to account for the kind of note obtained by percussion over the lungs, by supposing it to be due to the occurrence of resonance in the larger bronchial tubes. This theory is easily disproved by the facts that the lungs remain resonant when the larger bronchial tubes are filled with gelatine; and that when the alveoli are filled with coagulum, although the bronchi still contain air, the resonance is completely lost. The resonance of the lungs indeed, as Flint has maintained, is very similar to that of a loaf of bread, and depends on the physical properties of the tissue and on the character of the vibrations set up in it by percussion.

When percussion was first practised, the part of the body to be examined was struck directly by the fingers, or by a small hammer. This method was soon superseded by that now in vogue, known as mediate percussion, in which the stroke is made by the finger or fingers of one hand upon a plate of bone or other material, or more commonly upon one of the fingers of the other hand applied to the part of the body under examination.

In the analysis of the percussion sound as usually produced, then, there are three elements which have to be taken into consideration: (α) the sound produced by the impact of the percussing finger on the one percussed; (β) the sound produced by the vibration of the chest wall or of the abdominal walls or the wall of the stomach or intestines if the latter be tense; (γ) the sound produced by the vibration of the lung, or of the air in a cavity, such as a tubercular vomica, the pleura, stomach, or intestine, as the case may be.

The first sound will be clearly distinguished if one finger be percussed in the free air. It is a noise of feeble intensity and indefinite pitch. If now, instead of percussing the finger in free air, we do so holding it a a little distance above an open-mouthed jar it will at once become evident that the sound, though still of no great intensity, has become possessed of a definite pitch. If the experiment be tried with different jars the pitch will be found to vary with the jar; or if water be poured into a jar, the pitch of the note produced by percussion of the finger over its mouth will be found gradually to rise with the level of the water When the jar is filled the percussion note is as dead as it is in free air. Again, if one percusses over one's own mouth slightly opened it will be found that a note of a definite pitch is produced, which can be altered by altering the size of the buccal cavity.

The character which the percussion note acquires, when thus elicited over the entrance to a cavity, is due to what we have referred to as resonance properly so called. It results from the vibration of the air in a limited space in a definite manner, and the percussion throws the air into a certain mode of vibration fixed by the form of the vessel, and produces a note of definite pitch.

If the jar be held near the ear, and the corresponding note be sounded on an instrument, the note will be greatly intensified. The note to which the jar speaks will differ slightly from that of percussion, owing to circumstances which it is unnecessary to go into here.

The point on which I wish to insist is that the sound produced arises primarily from the vibration of the air in the cavity, and not from that of the walls of the cavity; although the latter by their vibration are capable of increasing and modifying the sound.

When the slightly distended stomach or a loop of intestine is percussed, a definite note is produced which similarly arises from the vibration of the contained air. The membrane, indeed, being slack, is not in the physical condition to produce a musical sound.

In the case of a superficially situated cavity in the lung the same result will be obtained, a clear note of definite pitch being produced.

In the case of a pneumothorax the air in the cavity will have a definite period of vibration and produce a definite note, and will combine with the sound produced by the vibration of the thoracic wall.

If the lung be percussed outside the body a sound is produced which closely resembles that of the ordinary thoracic sound. The resonant character of the note depends, as I have already said, on the spongy and elastic physical character of the lung-tissue.

The drum-like sound which occurs when the pleura is filled with air is modified, and becomes somewhat muffled, when the thoracic cavity contains the fully expanded lung.

The alteration which takes place when the pleura is partly filled with fluid is a very interesting one, and shows clearly the part taken by the vibration of the lung in the production of the percussion note. In such a case, if the upper part of the cavity were occupied by air instead of by lung, the note which would be elicited on percussion would be of much higher pitch than if the whole cavity were filled with air, and would be distinctly musical. Where the upper level is occupied by lung, the same is true; the lung is slack, there is no tension of the lung-tissue, and the air it contains vibrates almost as freely as if no lung-tissue were present. The note consequently is high-pitched although less pure, and less distinctly musical than it would be in the case of a cavity of corresponding size. This peculiarity in the percussion note above a pleuritic effusion is associated with the name of Skoda, who specially drew attention to it; the note is sometimes spoken of as *Skodaic.*

A variety of the percussion note which is frequently referred to is the *tympanitic.* This should properly denote the low-pitched full note which is obtained on percussion of the abdomen when the intestines are distended. The term, however, has been by some transferred to the rather high-pitched note elicited over a loop of gut which is not distended. This latter note closely resembles the Skodaic note, or that met with over a moderate-sized superficial pulmonary cavity.

In the case of a cavity in the lung where there is a free communication with a bronchus, the percussion sound not infrequently acquires a character spoken of as *pot fêlé* or "cracked pot." This is generally noticeable only when the percussion stroke is sudden and forcible and the patient holds his mouth open. The usual explanation given for this modification of note is that it is due to the sudden expulsion of the air in the cavity through the bronchus, which thus gives rise to a hissing or chinking sound superadded to the ordinary percussion sound. It may be produced when there is no cavity if the walls be yielding, as in the case of children, if the air be suddenly expelled from part of the lung by a sharp stroke.

The great value of the percussion note as a physical sign depends on the definite information which, as a rule, it gives about the structures underlying the spot percussed. We know that the only structures of the body capable of producing a resonant note are such as contain air. Normally the lungs, the air-tubes, the stomach and intestines only can give rise to a resonant note. Under abnormal conditions, air in the pleura, peritoneum, or in a cavity will produce altered resonant notes. When the note becomes dull we know there is little or no air present beneath the part percussed. In this way by percussion we are able to map out the superficial boundaries of tumours, of fluid effusions, or of solid organs surrounded by air-containing viscera. When there is a cavity, the peculiar quality already described which the percussion note assumes, helps in the recognition of its existence.

In the practical employment of percussion it must be borne in mind that there is no standard of resonance which can be applied to all cases. The percussion note on one side of the chest must be carefully compared with that on the other, and also the percussion notes at various points of the same side must be contrasted.

Auscultation.—Thus far we have been dealing with the sounds which are met with in percussion. We must now consider the sounds which are connected with auscultation.

A large proportion of these owe their origin to the movements of fluids through tubes and cavities. Such are the bruits met with in diseased conditions either of the valves of the heart or of the large vessels. Such are the normal respiratory murmurs and the abnormal sounds, crepitations, or rhonchi audible in disease; such, again, are the sounds to be heard on listening over the stomach and intestines.

Other sounds depend on the movements of one surface on another, as the friction sounds of pleurisy or of pericarditis.

We must therefore spend a little time in the consideration of the mode of production of these sounds. To M. Chauveau we are indebted for an elaborate experimental study of the conditions under which sounds are produced by fluid moving through tubes. His conclusions may be summarised as follows:—

(*a*) No sound is produced by a fluid flowing through a uniform tube or passing from a wider to a narrower one, whatever be the velocity of flow or whatever be the condition of the wall of the tube as regards smoothness or roughness.

(*b*) A sound may be produced when a fluid flows from a narrower to a wider space, and this sound will depend upon the velocity of flow and the relative size of the tubes.

These results are the outcome of observation and experiment. The statement that no murmur is produced in passing from a wider to a narrower tube has been shown by Bergeon to be too general. If the narrower tube have a lip projecting into the larger one it is capable, under certain conditions as to rate of flow, of producing a bruit.

With this exception the laws of Chauveau may be accepted as true and capable of general application.

The cause of the sound produced by a flow from a narrow to a dilated part is the formation of what is called a *fluid vein*, that is, a small portion of the fluid is set into vibration by the physical conditions under which it is placed. If now we apply these laws to the flow of blood in the vascular system we can state under what circumstances bruits will arise.

The flow of blood through the arteries will ordinarily be unattended with sound. If, however, pressure be exerted on the wall of an artery, so as to flatten it, a murmur will be produced at once by the blood flowing through the artificially narrowed portion to the wider part beyond.

In aneurysmal dilatation, a bruit may be produced by the passage of the blood through the dilated portion.

Similarly in the case of the veins no sound will ordinarily accompany the flow of the blood. Pressure on one of the larger veins, however, diminishing the lumen without stopping the flow, will produce the physical condition requisite for the production of a murmur. The existence of a communication between an artery and a vein will also be capable of producing a murmur.

As regards the heart and its valves, the relation of the orifices, the cavities, and the great vessels is such that ordinarily no bruit is produced by the motion of the blood itself. When the aortic valve is narrowed, or the aorta dilated just beyond the valve, then the passage of blood through the valve will be accompanied by a murmur whenever the velocity is great enough. The same will be true in the case of narrowing of the mitral or tricuspid valves.

When a chink is left in a valve, through imperfect closing, so that a stream of blood trickles back in the contrary direction, the physical condition for the production of a murmur is again satisfied.

Communications between the auricles or between the ventricles will also obviously admit of the generation of murmurs.

Next let us consider how and where bruits can be produced by the movements of air in the respiratory passages.

(i.) In inspiration a bruit may be produced at the external nares or naso-pharyngeal openings; at the mouth; at the glottis, and, as some think, also at the termination of the bronchiole in the alveolus. It is only with regard to the production of sound by the influx of air into the alveolus that any question can arise. On this point there is some difference of opinion, most authors believing firmly in the existence of an alveolar sound, while others hold that no sound can be produced in this way. When we consider the small, almost microscopic, size of the alveolus and of the bronchiole leading to it, the slightness of the current of air and the small velocity with which it can enter the alveolus, theoretical reasons appear very strongly to negative the possibility of any sound being produced in this way. The experiments of Chauveau and others, however, seem clearly to have established the fact that experimental obliteration of the glottic sounds does not annul the inspiratory sound heard by auscultation over the lungs. We are therefore forced to side with the majority in admitting the existence of an alveolar inspiratory sound resulting from the formation of innumerable small fluid veins.

(ii.) In expiration a bruit can be produced in the same situations as in inspiration except at the last-mentioned—the alveoli.

Further consideration of these bruits must be reserved until we come to deal with the subject of the conduction of sound.

We must next discuss what effects pathological conditions, such as consolidation of a portion of lung, can have in the production of sound in respiration.

In the case of consolidation, where the alveoli of a portion of the lung are completely filled with exudation, it is obvious no air can enter or leave the affected part. Whatever sounds, then, are audible over such a consolidated area must be conducted from other parts. That portion of the inspiratory bruit due to entrance of the air into the alveoli will be abolished. Is it possible that the passage of the air to and fro over the end of the tube leading to the consolidated part might produce a murmur? Theoretically this is possible; but it has been shown experimentally that if it occur at all it is to so slight an extent that in practice it may be neglected. Probably the volume of air and the velocity with which it moves are so small that ordinarily no murmur is produced.

In what way will the existence of a cavity in the lung influence the production of sound?

Here an important secondary question arises—the theory of resonance which has already been considered in part when dealing with percussion. The resonating property of a cavity will materially modify not only the sounds produced in the cavity but also those reaching it. There may or may not be entrance of air into the cavity and issue from it. Air may be drawn into the cavity during inspiration by the expansion of its walls, and expelled during expiration by their retraction; or the walls may be perfectly rigid and incapable of movement. The entrance of air into the cavity will be attended with the formation of a fluid vein and the production of a murmur, but its issue will not.

In the case where air is forcibly expelled from a cavity, as sometimes happens during coughing, the succeeding inspiration may be accompanied by a distinct suction sound produced by the sudden inrush of air into the cavity.

The discussion of the modification both in conducted sounds and in sounds locally produced in the cavity will be more appropriate after we have fully considered the subject of conduction.

We have next to consider what sounds owe their origin to the presence of secretions in the respiratory tubes: (i.) what will be the effect of the presence of a mass of mucus or thick secretion in one of the larger tubes

This condition will produce a local narrowing in the calibre of the tube, and therefore a murmur may occur both with inspiration and expiration. If the secretion be viscid, a projecting tongue may be formed capable of moving backwards and forwards and of giving rise to a snoring sound. It is obviously in the larger tubes only that such sounds can be produced; they are generally described as rhonchi, and are often distinctly musical.

(ii.) The presence of thin secretion through which air can bubble will produce quite a different sound. This will nearly always occur in the medium-sized tubes; in the smaller tubes a plug of mucus would be sufficient to prevent the entrance of air altogether. From its mode of production such a sound will generally be of a crackling character, in which case it goes by the name of crepitation. The different kinds of crepitations depend principally on resonance, and also on the nature of the tissues through which the sounds are conducted.

The production of sounds by the passage of liquid and air along the alimentary canal need not detain us long. Such sounds are similar to those we have been considering; but from the size of the tubes and the relative proportions of air and liquid they will be of a very different quality, and are more properly described as gurgling sounds. Sometimes they are so loud that they are audible at some distance from the patient.

Mention must be made of the splashing sounds which may be produced by shaking the patient, when air and liquid are simultaneously present in the pleura. This succussion sound, the origin of which is sufficiently obvious, is specially interesting as having been observed by Hippocrates.

The rubbing of two roughened surfaces together produces what is appropriately called a friction sound. It is generally met with in the case of pleurisy or pericarditis; but it may also occur over any of the larger viscera when the peritoneum is roughened.

It is said that in the case of the smaller bronchi or alveoli crepitation sounds may be produced by the separation of surfaces previously in contact, and it is quite conceivable that this may sometimes occur.

II. The conduction of sound.—The following may be stated as the laws which govern the conduction of sound so far as our subject is concerned.

(*a*) Sound emanating from a single source in a uniform medium diminishes in intensity according to the law of the inverse square of the distance. The same amount of energy acts on surfaces whose areas increase as the square of the distance. Thus if I be the intensity of the sound, d the distance of the source, E the amount of energy it gives out, we have

$$Id^2 \propto E,$$

or

$$I \propto \frac{E}{d^2}.$$

(*b*) Sounds are conducted by liquid and solid media as well as by air. The same law is followed as regards intensity as long as the media remain uniform. The velocity with which sound travels varies with the medium in which it is propagated.

(*c*) When sound travelling in one medium meets the boundary of another medium it is partly reflected and partly transmitted. Sound, propagated in a medium such as air is very badly transmitted to another of a very different character, such as a liquid or a solid.

(*d*) When sounds are produced by the movements of fluids through orifices they are best conducted in the direction in which the currents flow.

(*e*) Sounds may be conducted to great distances by tubes, rods, or wires, by means of which dissipation of energy is prevented. The sectional area remaining practically the same, the law of the inverse square does not come into operation. In the case of the tube, the sound is conducted by the air in its interior and not as a rule by its walls. The walls of the tube must be of sufficient thickness to prevent energy leaving it transversely. In the case of the rod and wire the sound is conveyed directly along the wood or metal of which they are composed.

A tube is specially adapted for the conduction of sounds of low intensity, such as whispered voice sounds, breath sounds and vascular murmurs. As is well known, the speaking-tube will conduct the whispered voice a long distance.

Stethoscopes are either solid rods, or tubes, with end-pieces for application to the surface of the body, and ear-pieces for apposition to the ear.

The tubular form is nearly always used at the present time. The tube may be made of some rigid material such as wood or metal, or of some soft material such as india-rubber. The ear-piece may be single, adapted for one ear only; or double, so that both ears may be employed simultaneously, the sound being conducted by a tube to each ear.

We are now in a position to inquire how sounds produced in the interior of the body are conducted to the surface.

First, let us consider the sounds which are to be heard on auscultating the trachea. From what has already been said as to the production of sound it is clear that in this case, under ordinary circumstances, the glottic breath sounds only will be audible. The sounds produced at the glottis will be modified by resonance in the tracheal cavity. Their intensity is thereby increased, and they will acquire a character peculiar to the resonating cavity into which they are conducted. Expiration and inspiration will be about equally loud, and possessed of a harsh blowing character. To the glottic breath sounds, as audible over the trachea or one of the larger tubes, the name of "*tubular breathing*" has been given.

Next let us consider the conduction of the breath sounds to the lungs and thence to the surface of the body. The sounds are of such feeble intensity that they are inaudible unless the ear be applied close to the chest wall, or diffusion be prevented by the interposition of a stethoscope between the latter and the ear.

We shall take it for granted that the sounds ordinarily heard over the lungs are the sounds produced at the glottis modified by conduction, and supplemented by the sounds produced at inspiration by the entrance of air into the alveoli. With the lungs in the ordinary condition the law of the inverse square will be very approximately true. The smaller tubes, thin-walled themselves and surrounded on every side by thin-walled air-cells with which they freely communicate, do not answer the purpose of preventing the general diffusion of sound. The consequence is that if we take the main bronchus as a centre, and describe a series of spheres round it, we shall have a series of surfaces over which the intensity of the glottic sounds will, approximately, vary inversely as the radius. The glottic sounds should, therefore, be better audible when the chest walls are thin, when the pleura is not thickened, and the nearer the point of auscultation to the main bronchi.

The sounds produced by the entrance of air into the alveoli should everywhere be of about the same intensity. The result of these two sources of sound is to make the inspiratory sound considerably longer and louder than is the expiratory.

Consolidation of the lung acts in two ways—

(i.) As no air enters the alveoli of the affected part the alveolar part of the respiratory murmur will be abolished.

(ii.) The alveoli being filled with exudation, the glottic sounds will be much more perfectly conducted along the tubes, the dissipation of sound which occurred through the free communication of the tubes with the air-spaces being prevented. The result is that the glottic sounds are distinctly conducted to the surface, and are unmingled with any sounds of local origin.

The explanation we have given assumes the continued patency of the tubes, the alveoli alone being blocked. If the tubes also are blocked, not only will the consolidated lung not prove a better conductor than normal lung, but indeed it will not conduct quite so well, as has been shown experimentally. In this case the breath sounds will be either very faintly tubular or entirely absent.

When the lung is collapsed, the tubes are flattened and partially obstructed. Collapse will, however, bring about a result which consolidation does not; and that is the approximation of the larger bronchi and the surface, as the result of which tubular breathing may be more or less clearly audible. In some cases the breath sounds may be entirely suppressed.

Emphysema is a condition in which, through dilatation of the alveoli and impairment of their elasticity, a lessened amount of air enters and leaves the lungs. The alveolar part of the respiratory sound is therefore diminished, while there is increased dissipation of the glottic part.

When a large bronchus is blocked by a foreign body, or is completely obstructed by external pressure, the only sounds which can reach the ear must come from the tubes on the laryngeal side of the obstruction. These, from the nature of the case, will be very badly conducted, and will be almost, if not quite, inaudible.

The presence of a cavity in the lung, communicating freely with a bronchus, will make an important modification in the sounds.

(α) Suppose air neither enters nor leaves the cavity during respiration. The dense walls of the cavity will prevent the diffusion of the sounds conducted from the bronchus; they can therefore reach the ear with increased distinctness.

(β) Practically in most cases air will enter and leave the cavity during respiration. We already have considered what effect this will have on the production of sounds.

Sometimes the amount of air entering will be so small that the sound so produced may be neglected. The glottic inspiratory sound may thus be augmented by the whiff, if any, produced by the entrance of air into the cavity, while no alteration will take place in the expiratory sound, which will be purely conducted glottic.

Frequently it will be quite impossible to say from the character of the breath sounds whether we are dealing with consolidated lung permeated by patent or dilated bronchi, or with a cavity. The breath sounds audible over a cavity may, however, have a certain distinctive character, in which case they are frequently spoken of as *cavernous* or *amphoric*. This quality is like that resulting from blowing over a bottle or jar. It has been explained as due to resonance or to reflection of the sounds at the walls of the cavity.

In discussing the percussion note we pointed out that in the case of a cavity the air contained by it is capable of vibrating so as to produce a note possessed of a definite musical pitch, although of no great intensity unless the vibration setting it in motion be correspondingly great. In the same way any sounds conducted to the cavity or produced in the cavity will, when it is of sufficient size and of definite shape, take on the note quality peculiar to the cavity. The breath sounds will then acquire that peculiar resonance quality which gives pitch and timbre to them, and makes them cavernous or amphoric.

In the same way this property of resonating will give the definite cavity quality to sounds otherwise essentially unmusical, such as crepitations. In the case of a large cavity, such as a pneumothorax, or one involving the greater part of a lung, the corresponding sounds will be proportionally loud and will have definite musical pitch. In this way crepitations frequently acquire a metallic character.

Of the same nature is the *bell sound* or *bruit d'airain*. This is observed when percussion is employed over a large cavity, or a pneumothorax, by means of two coins, one of which is held in contact with the chest and is percussed with the other. The sound so produced excites resonance in the cavity, and a peculiar metallic clink may be heard on auscultation with the stethoscope.

What is the effect of fluid in the pleura on the conduction of the breath sounds?

1st. Fluid in the pleura is necessarily attended with collapse of the part of the lung subjected to the pressure of the fluid, and consequently the only sounds which can be audible will be conducted glottic.

2nd. The interposition of a layer of fluid between the lung and the surface will undoubtedly cut off a considerable portion of the sound, and may succeed in cutting it off altogether.

In ordinary cases, at the upper margin of the fluid the breath sounds will be faintly tubular; at the lower part they will be almost, if not quite, annulled.

In the case of air in the pleura, the problem will differ according as there is or is not a fairly free communication with a bronchus. In the absence of adhesions the lung becomes collapsed. Whatever sounds are heard will be purely conducted glottic. If the communication of the bronchi with the pleural cavity be free, then tubular breath sounds, augmented by resonance and probably thereby invested with metallic quality, will be audible. If, on the other hand, communication with the bronchi have ceased, then such breath sounds as may be audible will be extremely feeble.

We may now consider very briefly what laws govern the conduction of the spoken and whispered voice sounds to the surface of the chest. The spoken voice sounds are produced at the larynx, and are modified and augmented by resonance in the cavities of the mouth and nose. The whispered sounds are produced by the lips, tongue, etc., and not at the larynx. We have already observed that whispered sounds are exceedingly well conducted by means of tubes. It therefore happens that whatsoever promotes the conduction of the laryngeal breath sounds will similarly assist the conduction of the whispered sound. Ordinarily the whisper will be very little audible over the chest wall. It will be well conducted, however, wherever there is underlying consolidation with patent bronchial tubes or a cavity opening into a bronchus : in the latter case it may acquire the cavernous quality. It may be audible over the upper part of an effusion, but will be absent at the lower part.

The spoken voice sounds will be conducted well or badly under similar circumstances. As they are of considerable intensity they have the power of throwing into vibration the tissue through which they are conducted. In the case of consolidation of the lung-tissue with patent bronchi, in consequence of the increased conduction of the voice sounds there will be increased vibration, which can be distinctly felt on the surface on application of the hand. The opposite is the case where there is effusion of fluid. The voice sounds are then badly transmitted, and the vocal fremitus to be felt by the hand is greatly diminished, or may be absent altogether.

Here I must refer very briefly to a modification of the voice sounds which is sometimes observed in cases of pleural effusion. When auscultation of the voice is practised about the upper level of the fluid it is found that it has acquired a peculiar bleating quality ; a modification usually spoken of as *ægophony*. No completely satisfactory explanation of this phenomenon has yet been given. The explanation most generally received is that of the late Dr. Stone, who found that when a pure tone was produced by the patient by means of a pitch-pipe there was no ægophony. The ordinary spoken voice is a compound sound composed of fundamental tones and their harmonics. Low tones are known to travel from air to liquid with greater difficulty than higher tones. A sound composed of a tone and harmonics will be altered on passing through the fluid by the deadening of the fundamental, the higher harmonics in consequence becoming relatively louder.

On the conduction of the adventitious sounds, such as *rhonchus* and *crepitation*, only a few words are necessary. Rhonchi, being produced in the larger tubes, usually in the trachea, will be audible all over the chest wall. Crepitations, on the other hand, arising in the smaller tubes will, as a rule, be audible only over the limited portion which is supplied by these tubes. As crepitations usually arise under conditions which are associated with consolidation, the former are generally conducted clearly to the surface, for the same reason that the breath and voice sounds are so distinctly conducted. When a cavity exists, crepitations excite resonance, and then frequently acquire a metallic character.

In the consideration of the heart sounds, normal and otherwise, the question of conduction is not of so much importance, and the laws which govern their conduction need not detain us long. Murmurs produced by the formation of fluid veins are conducted in the direction of the current. Hence the murmur due to mitral incompetence is conducted towards the left auricle, and is therefore generally audible towards the axilla as well as at the apex of the heart. The murmur due to aortic stenosis will be audible not only at the base of the heart but also in the direction of the great vessels. The murmur due to aortic incompetence will be conducted down the left ventricle, and often be well heard along the left border of the sternum.

The heart sounds will often be well heard over a pulmonary cavity or consolidation, in the case of the cavity being augmented by resonance. In such cases the cavity or consolidated lung must be closely connected with the heart or great vessels.

Friction sounds, such as those of pleurisy and pericarditis, are already superficial, and their conduction is a very simple matter. They are usually audible at and near the place of production.

The recent discovery of the *Röntgen rays* has greatly extended the possible range of vision as regards the interior of the body. If we cannot actually see internal structures, their shadows may sometimes be made visible. This depends upon the fact that when the rays pass through a body of varying density, the denser parts offer more obstruction to the passage of the rays than the rarer, and thus cast shadows which may be made visible on a sensitive screen or be permanently recorded on a photographic plate.

In the case of the hands and feet, where the parts are thin, the bones cast well-defined shadows, and thus are clearly shown on the screen or in a photograph. Foreign bodies in such parts may also be readily made manifest.

Where the parts are thick, as in the case of the thorax and abdomen, the shadows are much less well defined, but broad effects may be obtained. Thus the healthy lung is very transparent to the rays as compared with a consolidated lung, a new growth, a pleural effusion, or a hydatid cyst The latter, therefore, may give evidence of their presence by casting relatively darker shadows on the screen. The presence of an aneurysm with its pulsations may similarly be revealed by the shadow it casts. The application to the investigation of abdominal diseases presents great difficulties which have not yet been surmounted.

It may be pointed out, in connection with what has been said relating to percussion, that dulness on percussion goes along with bad transmission of the Röntgen rays, while resonance is accompanied by good transmission.

Thus it is found that, as a rule, wherever there is dulness to percussion there is shadow as compared with areas in which there is resonance; the intensity of the shadow being proportional to the degree of dulness.

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REFERENCES

1. AUENBRUGGER. *Inventum novum ex percussione thoracis humani ut signo abstrusos interni pectoris morbos detegendi.* Vindobonæ, 1761. (Translation by Corvisart, Paris, 1808.)—2. BARIÉ, E. *Bruits de souffle et bruits de galop.* Paris, 1894.—3. BERGEON. *Des causes et du mécanisme du bruit de souffle.* Paris, 1868.—4. BESNIER. "Matité," *Dict. encycl. d. sc. méd.* Paris, 1872, v. 212-227.—5. BULLAR, J. F. "On the Percussion of the Lungs and Chest," *St. Barth. Hosp. Rep.* Lond. 1883, xix. 211-220.—6. CARY, C. "The Production of Tubular Breathing in Consolidation and other Conditions of the Lungs," *Tr. Ass. Am. Physicians*, Phila 1892, vii. 313-323.—7. CASTEN, E. "Note sur une loi fondamentale dans la théorie de l'auscultation," *Compt. rend. Soc. de biol.* Paris, 1894, 10 s. i. 805-807; *Arch. de physiol. norm. et path.* Paris, 1895, 5 s. vii. 225-238.—8. CHAUVEAU, A. "Études pratiques sur les murmures vasculaires ou bruits de souffle et sur leur valeur séméiologique," *Gaz. méd. de Par.* 1858, 247, etc.—9. COIFFIER. *Précis d'auscultation*, 2nd ed. Paris, 1890.—10. FLINT, A. "The Analytical Study of Auscultation and Percussion with Reference to the Distinctive Characters of Pulmonary Signs," *Tr. Internat. M. Cong.* 7 sess. Lond. 1881, ii. 130-141.—11. GALLIARD, L. "Le bruit de pot fêlé," *Méd. mod.* Paris, 1895, vi. 597-601.—12 GEE, SAMUEL. *Auscultation and Percussion*, 4th ed. Lond. 1893.—13. *Idem.* "The Theory of the Breathing Sounds heard by Auscultation," *St. Barth. Hosp. Rep.* Lond. 1890, xxvi. 103-105.—14. GUTTMANN, P. "Percussion," *Real-Encycl. d. ges. Heilk.* Wien u. Leipz. 1882, zehnter Band, 442-465.—15. *Idem.* *A Handbook of Physical Diagnosis.* Translated by A. Napier, M.D., London. The New Sydenham Soc. 1879.—16. LAENNEC, R. T. H. *Traite de l'auscultation médiate et des maladies des poumons et du cœur*, 2nd ed. Paris, 1826. (Translation by Sir John Forbes, 4th ed. Lond 1834.)—17. LEREBOULLET, L. "Percussion," *Dict. encycl. d. sc. méd.* Paris, 1886, xxii. 733-760.—18. LYON, T. GLOVER. *The Thoracic Percussion Note.* Thesis for M.D. Cantab. 1885.—19. NOORDEN, C. v. "Auscultation," *Real-Encycl. d. ges. Heilk.* Wien u. Leipz. 1894, drit. Aufl. zweiter Bd. 536-559.—20. SIMON, P. *Manuel de percussion et d'auscultation.* Paris, 1895.—21. SKODA, JOSEPH. *Abhandlung uber Perkussion und Auscultation.* Wien, 1839. (Translation by W. O. Markham. Lond. 1853.)—22. STEINTHAL, C. F. *Experimentelle und klinische Untersuchung uber die Ursachen des vesicularen Athmungsgerausches.* Heidelberg, 1885.—23. STONE, W. H. *St. Thomas's Hospital Reports*, 1871, ii. 187.—24. TAYLOR, F. "On the Causation of Ægophony," *Med.-Chir. Trans.* Lond. 1895.—25. VIERORDT, H. *Kurzer Abriss der Percussion und Auscultation*, 4. Aufl. Tubingen, 1895.

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most marked in the early stages of cirrhosis before the portal obstruction has become very excessive. It would appear more probable, therefore, that cirrhosis and splenic enlargement are due to the same cause, and not that the splenic change is purely mechanical and secondary to the portal obstruction. This perhaps is not exclusively the case, for when the splenic vein becomes thrombosed the spleen is considerably increased in size; in an example which came under my observation it weighed 36 oz.

If, however, any toxic or septic condition be added to mechanical congestion, the organ may enlarge and become softened. This is well seen in infective endocarditis, where the diffluent enlarged condition of the organ contrasts with the cardiac spleen already described as resulting from backward pressure alone.

Hæmorrhages.—In an examination of 150 still-born children, Dr H. Spencer found a large number of visceral hæmorrhages in various organs, due apparently to damage received during delivery. The spleen only showed hæmorrhages in three cases; which is perhaps accounted for by the small size, mobility, and extensibility of the organ. In later life, traumatism may give rise to hæmorrhages into the substance of the organ.

Small hæmorrhages into the pulp of the organ are commonly seen in bacterial infection.

Cysts.—*Hydatid.*—The spleen is but seldom occupied by hydatid cysts; according to Thomas, in only 2 per cent of cases of hydatid disease. In 45 cases it was the only seat of echinococcus cysts, and in 43 other cases collected by him other organs were also involved. In 37 out of these 43 cases the liver was also involved. In half the cases of hydatid disease of the spleen no symptoms were noticed, and the cyst was only discovered post-mortem.

The contracted remains of spontaneously cured hydatid cysts are sometimes found.

Dermoid cysts are very rare indeed.

Serous cysts with clear contents are very rarely met with. Small cysts on the surface, when associated with thickening of the capsule, may possibly be explained as dilated lymphatic vessels; or possibly as some fragments of the peritoneal endothelium becoming included inside the organ and subsequently giving rise to cystic spaces.

Cysts containing blood or the débris of extravasated blood may sometimes follow traumatism.

Pilliet thinks that blood-cysts may be derived from angiomata in the spleen, the surrounding pulp yielding and giving way (42).

Mr. J. K. Thornton removed a spleen containing a multilocular cyst with 30 oz. of blood-stained fluid, in which there was much cholesterin, from a girl aged nineteen years. There was no evidence of previous traumatism. Microscopically the process of cyst-formation appeared to be due partly to breaking-down of the Malpighian bodies, and partly to plugging of vessels and destruction of the organ.

Innocent tumours, apart from cysts, hardly ever occur; the presence of fibromata apparently in the substance of the organ, and not the common lamellar fibromata of the capsule, is referred to by some authors.

Infarcts.—Clinically infarcts of the spleen manifest themselves by pain and tenderness in the splenic region, chiefly due to the accompanying local peritonitis, and by some enlargement of the organ. Occasionally there may be sudden and severe pain, presumably at the time that the embolus becomes impacted in the vessel. As a result of the subsequent absorption of the necrosed splenic tissue the temperature is raised.

Causes of infarction.—Fragments of blood-clot or vegetations dislodged from the valves or endocardium of the heart are the most frequent source of embolism of the splenic artery. The same result may follow detachment of particles of calcareous material set free from sclerosed valves or from atheromatous patches in the aorta.

These emboli are divisible into two kinds—(i.) infective, those which contain pyogenetic micro-organisms, such as are present in cases of infective endocarditis or, much more rarely, in infective arteritis. Such emboli give rise to suppurating infarcts, and the process is essentially the same as that of a pyæmic abscess in the organ; (ii.) simple or non-infective emboli which give rise mechanically to anæmia, necrosis, and the changes of a simple infarction.

Besides embolism there are other forms of interference with the circulation which may result in the production of an infarct. Thrombosis in the branches of the splenic artery may have this effect, as is sometimes seen in typhoid, typhus, and relapsing fever; and commonly in the greatly enlarged spleens of leukæmia.

Occasionally thrombosis of the trunk of the splenic vein may give rise to multiple infarcts. In two instances that have come under my own observation, the resulting infarcts have been anæmic and not hæmorrhagic. It might, perhaps, have been naturally expected that complete thrombosis of the splenic vein would have led to a hæmorrhagic infarct, as in Litten's experiment of ligature of the renal vein.

Morbid anatomy of a splenic infarct.—The terminal branches of the splenic artery do not anastomose with each other except by capillaries, each of them supplies exclusively a definite area of the spleen, they are therefore called end arteries. When one of these terminal branches has been recently blocked by a simple non-infective embolus, the area of the spleen supplied by it becomes anæmic, and the condition is a white or anæmic infarct. This is what is commonly seen in the spleen; but occasionally this condition of anæmia becomes succeeded by one in which the area is full of blood, a red or hæmorrhagic infarct.

The affected area is roughly triangular, the apex being towards the hilum of the organ, and corresponding to the occluded artery and the base towards the capsule. A thin area of healthy splenic tissue can usually, however, be seen immediately under the capsule which, together with the capsule itself, is nourished by the capsular arteries of the organ.

The anæmia is succeeded by coagulation necrosis; the affected area becomes somewhat swollen or infarcted, projects slightly above the surrounding surface of the organ, and is of a dull white colour.

If a recent white infarct is compared with the whitish yellow scar left by an old infarct, it will be seen that the cicatrisation and contraction of the old infarct have led to a depression; while the recent infarct is on a level with or even projects above the surrounding surface.

When an anæmic becomes a hæmorrhagic infarct the blood first distends the vessels, which, however, from malnutrition are unable to contain it, and allow it to deluge the affected area. This engorgement of the vessels Cohnheim regarded as due to a regurgitation of blood from the veins of the adjacent areas, which, unlike the arteries, do anastomose. Litten's experiments, however, pointed strongly to the blood being derived from the arteries running in the capsule of the organ and not from the veins.

Following on coagulation necrosis and its accompanying fatty degeneration, and probably as a result of the irritating property of the fluids derived from the necrosed cells, inflammation is set up around the infarction. This is shown by a zone of congestion in the substance of the organ, and by local peritonitis on the surface. This inflammation leads to an invasion of the infarcted area by young connective tissue cells, phagocysts, and so forth; and the processes of replacement fibrosis and absorption of the necrosed tissue take place side by side. Eventually a depressed cicatrix is left, with perhaps in the centre, if the infarct be large, some encapsuled caseous débris, the remains of necrosed tissue which was too extensive to be absorbed.

Occasionally calcification of the cicatrix of the infarct may occur.

The local peritonitis may produce loose tags of fibrous tissue, or adhesions to adjacent organs, to the omenta or to the diaphragm.

When an infective embolus lodges on the spleen, the first stages are the same as those described above for a simple embolus; and sometimes in infective endocarditis a definite anæmic infarct may be seen before the subsequent acute inflammation and suppuration have supervened. This soon passes into a pyæmic abscess.

Abscess.—The softened and often diffluent condition of the spleen seen in cases of bacterial infection may be described as a splenitis, and is in some degree comparable to lymphadenitis. This condition of the spleen is commonly seen in infectious fevers, but very rarely indeed goes on to suppuration in these diseases.

The causes of abscess in the spleen.—One of the most frequent causes of splenic abscess is infective endocarditis. In association with this disease the spleen is enlarged and softened, in short, in the condition seen in bacterial infection. When an abscess occurs it is the result of septic embolism in the organ, giving rise first to an infarct which, instead of running the course of an ordinary infarct, breaks down, while extensive suppuration is set up by the micro-organisms contained in the embolus.

Such an infarct in the earliest stages may be anæmic or hæmorrhagic, but softening and suppuration soon supervene.

In pyæmia, abscesses embolic in origin, like those in infective endocarditis, are often met with. Thus Stephen Paget in 430 cases of general pyæmia found abscesses in the spleen in 39.

In pylephlebitis abscesses may form in the spleen, but this is very rare as compared with abscesses in general pyæmia. S. Phillips found three abscesses in a spleen weighing 38 oz., in which suppurative phlebitis of the portal vein was due to perforation of the mesenteric veins by a bristle. In suppurative pylephlebitis the abscesses in the spleen are not necessarily always due to the direct spread of the inflammatory process along the splenic vein, but may be due to general pyæmia and septic emboli carried by the arteries.

Suppuration in the spleen has, in rare instances, occurred in typhoid fever; it has been shown to be due to the activity of the typhoid bacillus, and may be due to secondary infection with other micro-organisms. Infarcts, as mentioned above, are found very occasionally in typhoid fever; they may slough, and thus give rise to an abscess.

Splenic abscess has also been recorded as a result of malaria, but is probably due to a secondary infection by pyogenetic micro-organisms.

Extension of inflammation from adjacent parts usually only sets up peritonitis on the surface of the spleen; but a perforating ulcer in the stomach or colon may penetrate the spleen, and give rise to suppuration in the organ.

Hydatid cysts of the spleen are rare; if suppuration occurred in a cyst embedded in the organ it would closely resemble a splenic abscess.

Injury has been the only discoverable cause of some splenic abscesses; it probably acts by reducing the resisting power of the organ, and so giving free play to any pyogenetic micro-organisms present.

A number of cases have been described in which no definite cause for splenic abscess was forthcoming; some of these cases were probably pyæmic and embolic in origin, and secondary to suppuration elsewhere. Thus, like cerebral abscess, suppuration in the spleen may be secondary to inflammation and suppuration in the thorax.

A softening gumma, and perhaps actinomycosis, may give rise to the appearances of an abscess in the spleen. Actinomycosis, however, when it attacks the spleen generally produces a firm growth somewhat like an anæmic infarct.

Tuberculosis.—*Generalised tuberculosis.*—In this condition the spleen, like other organs, becomes infiltrated with miliary tubercles.

They are much more evident on the capsule than in the substance of the organ, where there is moreover some difficulty of distinguishing them by the naked eye from Malpighian bodies. On the surface they appear as gray, rarely as yellow points; occasionally they may set up local peritonitis, and may even give rise to the formation of a fibrinous membrane on the surface of the organ. On section of the organ, gray miliary tubercules can, according to Sir S. Wilks, be distinguished from Malpighian bodies by the fact that, when exposed to a stream of water, the normal splenic tissue is dislodged sooner and more easily than the *tubercles which cling to the trabeculæ. In generalised tuberculosis the spleen is enlarged and soft; when of rather older date, the tubercles may caseate while still remaining discrete.*

Chronic tuberculosis.—Large caseous masses, though common in the spleens of animals, are by no means common in man; when they do occur, they are more often met with in children than in adults.

Large, round, caseous masses, with some smaller miliary tubercles near them, are somewhat loosely embedded in the spleen substance. After a time they soften down in the centre, and can then be recognised at once. Caseating tuberculous material, before it has softened down, cuts with a firm section, and to the naked eye so closely resembles the "hard-bake" spleen of chronic or hard lymphadenoma that a microscopic examination may be required to distinguish between them.

The caseous masses are not, as a rule, surrounded by fibrous tissue; but in cases of exceptional chronicity the spleen may be extensively fibrosed, and so pigmented as to resemble lymphadenoma; especially when there is little caseation. Calcification may occur in the caseous tuberculous patches.

Microscopically, giant cells are usually abundant; but the giant-cell system is often incomplete, and the demonstration of tubercle bacilli may be difficult.

Syphilis.—*Acquired syphilis.*—During the exanthem the spleen is often found to be enlarged, presumably as the result of the local action of the syphilitic toxin.

In the tertiary stage gummata are rarely met with; Dr. Still has only been able to collect twenty recorded cases. When present, they may reach a very large size; thus, in a case recorded by Drs. Delépine and Sisley, one-third of the spleen, which, though it was not lardaceous, weighed 38 oz., was occupied by a large gumma; numerous smaller gummata were present, and there was general fibrosis of the organ.

Over a gumma capsulitis and adhesions to the diaphragm and adjacent parts are found, especially if it impinges on the surface. Apart from gummata capsulitis is often found in the bodies of syphilitic subjects. Cicatrices involving the substance of the organ may result from gummata which have undergone absorption.

As a consequence of syphilis lardaceous change in the spleen often results.

In *congenital syphilis* the spleen is generally enlarged, and firmer than normal; sometimes the splenic enlargement is excessive and may be associated with hepatic enlargement. Dr. Gee found enlargement in one-fourth of all cases of hereditary syphilis.

Structurally there may be a general fibrosis, sometimes attacking the pulp especially, at other times radiating from the fibrous trabeculæ.

Lardaceous disease may occur as in acquired syphilis. Gummata appear to be very rare, rarer perhaps than is usually thought; Dr. Still was only able to collect six cases in children. Of these, four occurred in late hereditary syphilis between the ages of six and eleven years, and the other two in early infancy. In four of the cases there were gummata in the liver, and in a fifth in the kidney. In none of the cases was there a solitary gumma in the spleen; usually they were numerous, and in three miliary.

Rickets.—The spleen is generally regarded as enlarged in rickets; thus T. Colcott Fox and Ball record sixty-three cases of enlarged spleen in children, all of whom were rickety, and quote Gerhardt, who found splenic enlargement in thirty-five out of fifty-four rickety children, and Kuttner, who found it forty-four times in sixty cases of rickets; lower estimates put it at 40 per cent.

On the other hand, Henoch, Donkin, and V. Starck regard enlargement of the spleen in rickets as merely accidental, and not due to the same cause that produces the skeletal and other characteristic features of the disease.

The enlargement may in some cases be apparent rather than real, and due to downward displacement of the organ as the result of rickety deformity of the thorax. In other cases some other disease may have been present; thus, in one of Sir W. Jenner's cases of "albuminoid" change in rickets, the spleen of a very anæmic boy, barely two years of age, weighed 9½ oz.; the details of the case are quite compatible with the view that he had splenic anæmia in addition to rickets. The enlargement of the spleen can also be explained as the result of some toxic absorption from the intestines, or lungs, which, in rickets, are both frequently in a condition of catarrhal inflammation. Dr. Hogben ascribed a form of biliary cirrhosis in the livers of rickety children to this cause, and the hypothesis might be extended to explain any fibrosis that might chance to be found in a rickety child's spleen. To sum up, the spleen is frequently found enlarged in rickets, but it is of no special importance, and presents no definite pathological lesions.

Lardaceous disease.—The spleen seems to be the organ most frequently attacked; thus, in fifty-eight cases of lardaceous disease tabulated by Dr. F. C. Turner, the spleen was involved forty-eight times, the liver thirty, the kidneys fifteen, and the intestines ten. In twenty-three of these cases the spleen was the only organ invaded.

Lardaceous disease attacks the spleen in two ways:—

(i.) The "sago" spleen; the capillaries of the Malpighian bodies are the parts affected, the arteriole in the centre of the corpuscle being as a rule healthy. The Malpighian bodies are enlarged to three or four times their normal size, and, being translucent, to the naked eye resemble grains of sago. The pulp and the lymphoid cells are unaffected. The sago spleen is firm, somewhat anæmic, and increased in size.

(ii.) The diffuse, waxy spleen, uniformly lardaceous or bacony spleen. This is much less common than the sago spleen. The chief changes are in the walls of the blood sinuses, which become much thickened and swollen. The lining endothelium is not affected. The small arteries are affected, but the trabeculæ remain unattacked. The Malpighian bodies are unaffected, or affected but rarely; they may be present, but more often they have disappeared. The splenic pulp becomes lardaceous secondarily. The diffuse, waxy spleen is enlarged, and is heavier than the sago variety, it is resistant, and presents a dry surface on section.

For a detailed account see article on "Lardaceous Disease," vol. iii. p. 255.

Malignant disease of spleen.—It is doubtful whether primary carcinoma of the spleen ever occurs. In 1886 Notta collected nine cases, and gave a clinical account of a case, in which, however, no post-mortem examination was made. It may possibly have been a sarcoma of the left kidney with secondary growths in the spleen and liver, inasmuch as the first symptom was hæmaturia.

A few cases have been described, which, like Gaucher's (20) *l'epithéliome primitif de la rate*, are probably examples of the splenic lesion of splenic anæmia. Recently Picou and Ramond have given a careful account of this condition, and regard it as a carcinoma derived from pancreatic cells included in the spleen during fœtal life. They had seen such cells in a three months' fœtus, and Peremeschko had described the same appearance in the spleens of embryos, young children, and suckling women. This hypothesis is a reasonable explanation of the presence in the spleen of a tumour thought to be carcinomatous; but it cannot be said that the existence of primary carcinoma of the spleen has yet been positively proved.

In Picou and Ramond's case an enlarged spleen was removed by laparotomy from a woman who had been ill for four years; it contained large cells 16-30 μ, with nuclei 4-8 μ. A similar appearance is described by Collier in the enlarged spleen of a child who had been ill for two years. Clinically, the long duration of the disease and the general resemblance to splenic anæmia are against the malignant nature of the change in the spleen, and in favour of its being the lesion of chronic splenic anæmia. Gaucher (21), in fact, in Debove and Bruhl's description of splenomegalie primitive or splenic anæmia, recognised the condition which he had previously called *l'epithéliome primitif de la rate*. Moreover, from a pathological point of view, the large cells resemble those seen in chronic inflammatory conditions of lymphatic tissue. This enables us to explain the fact that in Ramond and Picou's case the adjacent glands in the hilum of the spleen showed the same characteristically large cells, without being driven to the conclusion that the splenic condition was necessarily carcinomatous because there was a secondary growth in the adjacent lymphatic glands. In other instances, as in a case reported on by the Morbid Growths Committee of the Pathological Society (3), and found to be carcinoma, the possibility of a primary growth has not been definitely excluded.

With regard to primary sarcoma of the spleen, there is no *a priori* reason against its occurrence, as there is against primary carcinoma. Possibly it may occur, Hamilton says that it undoubtedly does; but it must be extremely rare. Dr. Norman Moore has described a mixed-celled sarcoma of the spleen which grew directly into the stomach, and Weichselbaum a fibro-sarcoma.

A pulsating cavernous angioma with a secondary growth on the liver has once been seen.

Secondary growths are by no means frequent in the spleen. Thus, in 735 autopsies of carcinoma of the mamma the spleen was the site of secondary growths in seventeen cases; and in 244 cases of cancer of the uterus there was only one case in which a secondary nodule was found in the spleen (39). Of 161 cases of carcinoma of all parts of the body collected from the post-mortem records of St. George's Hospital by Dr. A. Walker, secondary growths were met with in the spleen in seven, while in fifty-four cases of sarcoma from the same source there was but one instance of a secondary splenic growth.

In fifty cases of melanotic sarcoma quoted by Von Ziemssen the spleen contained secondary growths in thirteen.

In cases of carcinoma of the cardiac end of the stomach the spleen may become invaded by continuity of growth; it may also, of course, become infected from the surface in cases of general malignant disease of the peritoneum.

For spleen in *malaria*, *lymphadenoma*, *splenic anæmia*, and *leukæmia* the reader is referred to the special articles on those subjects.

Wandering spleen is dealt with in the article on "Enteroptosis."

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REFERENCES

1. Adami. *Montreal Medical Journal*, August 1896.—2. Albrecht. *Wien. med. Woch.* May 2, 1895.—3. Arnott, H. *Trans. Path. Soc. London*, vol. xxiv. p. 222.—4. Ballance. *Brit. Med. Journal*, 1897, vol. i. p. 145.—5. Bardach. *Ann. de l'Inst. Pasteur*, vol. iii. p. 577.—6. Biggs. *New York Path. Soc.* Oct. 11, 1893.—7. Bottazzi. *Archives ital. de biolog.* 1895, p. 462.—8. Bruhl. *Archives gén. de méd.* 1891, vol. clxvii. p. 168.—9. Collier. *Trans. Path. Soc. London*, vol. xlvi. p. 148.—10. Copeman. *St. Thos. Hosp. Reports*, vol. xvi. p. 155.—11. Coupland. *Brit. Med. Journ.* 1896, vol. i. p. 1445.—12. Courmont and Dufface. *Compt. Rend. de biolog.* June 19, 1896.—13. Debove and Bruhl *Bull. et mém. méd. soc. des hôp. Paris*, 1892, p. 596.—14. Delépine and Sisley. *Trans. Path. Soc. London*, vol. xlii. p. 147.—15. Flexner. *Journal of Experimental Medicine*, vol. ii. p. 197.—16 Fox, T. C., and Ball. *Brit. Med. Journ.* 1892, vol. i. p. 854.—17. Friedrich. "Acute Splenic Tumours," *German Clinical Lectures*, New Sydenham Soc. vol. lxxi. 1877.—18. Gabbi. *Ziegler's Beitrage*, xix. p. 647.—19. Garrod. *St. Bartholomew's Hospital Reports*, vol. xxx.—20. Gaucher. *Thèse Paris*, 1882.—21. *Idem. Semaine médicale*, 1892, p. 331.—22. Gee, S. *Brit. Med. Journ.* 1867, p. 435.—23. Gueorgaievsky. *Gazeta Botkina*, 1896, pp. 1313, 1343, quoted in *La Presse médicale*, Jan. 30, 1897.—24. Hamilton. *Pathology*, vol. ii. part ii. p. 789—25. Hogben. *Birmingham Med. Review*, vol. xxiv. p. 65.—26. Hunter. *Lancet*, 1888, Sept. 22.—27. *Idem. Lancet*, 1892, vol ii. p. 1259.—27*a*. *Idem. Journal of Path. and Bacteriology*, vol. iii. p. 259.—28. Jolly. *Bull. Anat. Soc. Paris*, 1895, p. 745.—29. Jonnesco. *Progres médical*, No. 12, 1897.—30. Kanthack. *Centralblatt f. Bakt. u. Parasit.* xii. p. 227.—31. Kelynack *Birmingham Medical Review*, Feb. 1897.—32. Klein. *Trans. Path Soc. London*, vol. xxviii. p. 439.—33. Laudenbach. *Archives de Physiolog.* 1897, p. 385.—34. Moniouri. *Riforma Med.* 1893, p. 472.—35. Moore, N. *The Bradshaw Lecture* 1889, p. 46.—36. Mosler in Von Ziemssen's *Encyclopædia of the Practice of Medicine*, vol. viii. p. 349, English translation 1878.—37. Notta. *Archives gén. de méd.* 1886, i. p. 166.—38. Orlandi. *Riforma Med.* 1893, p. 195.—39. Paget, S. *Lancet*, 1889, vol. i. p. 571.—40. Phillips, S. *Trans. Clin. Soc.* vol. xxviii. p. 222.—41. Picou and Ramond. *Archives*

de méd. expériment et d'anat. path. 1896, p. 168.—42. PILLIET. *Compt. Rend. Soc. de Biolog.* Paris, 1895, p. 679.—43. *Ibid.* 1894, p. 331.—44. *Ibid.* 1892, p. 905.—45. PITTS and BALLANCE. *Trans. Clin. Soc.* vol. xxix. p. 102.—46. PRICE. *Guy's Hosp. Reports,* Series III. vol. xxvii. p. 295.—47. REIGNER. *Berlin. klin. Woch.* Feb. 20, 1893.—48. RIGHI. *Riforma Med.* 1893, p. 170.—49. ROLLESTON and FENTON. *Birmingham Med. Rev.* Oct. 1896.—50. STARCK. *Deutsches Archiv f. klin. Med.* lvii. p. 265.—51. SHATTOCK. *Trans. Path. Soc. London,* vol. xliv. p. 151.—52. SPENCER, H. *Trans. Obstet. Soc.* vol. xxxiii. p. 284.—53. SPENCER, W. G. *Lancet,* 1897, vol. i. p. 651.—53*a.* STILL, G. F. *Trans. Path. Soc. London,* vol. xlviii.—54. STOCKMAN. *British Medical Journal,* 1895, vol. ii. p. 1473.—55. SUTTON, J. B. *Trans. Clin. Soc. London,* vol. xxvi. p. 48.—56. THOMAS *On Hydatid Disease,* vol. ii. p. 21, 1894.—57. THORNTON. *Trans. Path. Soc London,* vol. xxxv. p. 385.—58. TICTINE. *Mediz obozrenie,* No. 18, 1893.—59. TIZZONI and CATTANI. *Centralblatt f. Bakt. u. Parasit.* xi. p. 325.—60. *Idem. Riforma Med.* 1893, p. 189.—61. TURNER, F. C. *Trans. Path. Soc. London,* vol. xxx. p. 517.—62. WASHBOURNE. *Trans. Path. Soc. London,* vol. xlvi p. 325.—63. WEICHSELBAUM. *Virchow's Archiv,* Bd. lxxxv. S. 562.—64. WELCH and FLEXNER. *Journal of Exper. Med.* No. 1, p. 1896.

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ADDISON'S DISEASE

SYNONYMS.—*Morbus Addisonii, Melasma Addisonii, Bronzed disease, Asthénie surrénale, Melanodermie asthénique.*

Definition.—An exaggeration of the normal pigmentation of the skin, associated with extreme prostration and a tendency to syncope, nausea and vomiting. During life no morbid lesion is discoverable, and post-mortem alteration of the suprarenal capsules is the chief or only change found.

History.—In searching for the cause of pernicious anæmia Thomas Addison of Guy's Hospital discovered the association between disease of the suprarenal bodies and the train of symptoms that bear his name.

This observation was first reported publicly in a paper (4) read in 1849 before the now extinct South London Medical Society; but it attracted no attention until 1854, when Addison (3) published a monograph of thirty-nine pages "On the Constitutional and Local Effects of Disease of the Suprarenal Capsules." The discovery was slow to receive general recognition, and in the prefatory remarks appended to the reprint of this paper on Addison's collected writings, published by the New Sydenham Society in 1868, eight years after his death, it is stated that "even now it (Addison's disease) does not find a place in the nosology of some writers."

To the loyal and unselfish efforts of Sir S. Wilks the general acceptation of this remarkable discovery is largely due; he collected, sifted, and described the clinical features and pathological details of numerous cases of the disease in the Guy's Hospital Reports (56).

Trousseau, in his widely-known clinical lectures, gave honour to whom honour is due in naming the morbid entity Addison's disease (52). The late Dr. Headlam Greenhow wrote largely on the subject, more especially in the Croonian Lectures on Addison's disease before the College of Physicians in 1875, in which he collected a large number of cases, and gave a very complete review of the subject, to which little was added for fifteen years.

Within the last few years the great advance on our physiological knowledge of the so-called ductless glands has led to corresponding interest and research in connection with their diseases. This has resulted in considerable attention being paid to the pathology and treatment of Addison's disease.

Comparatively little has been added to our knowledge of the clinical aspect of the disease since it was first described by Addison. The nature of the lesions found and the mechanism by which they lead to the symptoms characteristic of the disease have, however, been interpreted in different lights.

Addison in his original memoir considered that any lesion of the suprarenal bodies which interfered sufficiently with their function would give rise to the disease. Wilks narrowed down this broad conception, and insisted that all genuine cases of the disease are due to one and the same lesion, which he considered to be a primary inflammation of the suprarenal bodies homologous to hepatic cirrhosis; and that the symptoms were not due to the changes in the suprarenal bodies, but to the effects thus secondarily induced in the adjacent sympathetic. These views were endorsed by Dr. Greenhow, and for many years were accepted without demur.

Since the theory of the internal secretions of glands has become established on an experimental basis, and especially as a result of the work of Abelous and Langlois (1) in France, and of Schafer and Oliver (45) in this country, opinion has reverted, in a more definite form, to the view first expressed by Addison, that the symptoms are due to interruption of the functional activity of the suprarenal capsules.

Etiology.—The disease is decidedly rare; Osler (38) thinks it is even less common in America than in Europe. It occurs much more frequently in males; of 193 cases tabulated by Greenhow, 125 (or 65 per cent) were males, and 68 (or 35 per cent) females.

It occurs on an average at about thirty-one years of age, and is extremely rare late in life; while only a very few examples in infants have been recorded.

It does not seem to be proved that the disease is more frequently seen in tuberculous families, or that it is in any way hereditary. It is interesting, however, to note that Andrewes (8) has recorded two cases in brothers.

Tuberculous disease of the suprarenal bodies may be associated with tubercle elsewhere in the body, and may spread, by a process of extension, from tuberculous osteitis of the neighbouring lumbar vertebræ. Alexais and Arnaud (6) were able to refer to twenty-three cases of this association of morbid changes. On the other hand, the suprarenal bodies are often the sole site of tubercle in the body. Strains or injuries to the back and blows on the abdomen have seemed to be the cause of the disease; this may be explained by supposing that the injury so impaired the vitality of the organs as to render them vulnerable to the tubercle bacilli: or, again, traumatism may have given rise to hæmorrhage into the substance of the suprarenal capsules; the destruction of the glands, and the subsequent fibrosis, leading to the development of Addison's disease. Hæmorrhages into the suprarenal bodies, probably due to trauma, were found in 26 out of 130 still-born children examined by Dr. Spencer (47). Wainwright (54) has recorded the case of a child aged two months, in whom the organs showed changes probably due to imperfect absorption and organisation of blood extravasated into their substance. Possibly, in some instances, Addison's disease may be the result of extensive damage received from the extravasation of blood into their substance during birth; the slighter cases probably end in recovery, or no signs of the disease appear.

Greenhow was of opinion that Addison's disease was more rarely seen among the upper ranks of society than among the labouring classes, who are more exposed to injury. It must be remembered, however, that it is far from being a common disease; and that if its incidence in the labouring and leisured classes were proportionately equal we should see many more cases among the former.

Morbid anatomy.—*Condition of the suprarenal capsules in Addison's disease.*—In Addison's original paper (published in 1854) 11 cases are recorded; in five of these cases there was caseous tubercle in both suprarenals, and in one case tubercle was present in one suprarenal. One case (No. 4) appears to have been an example of cirrhosis and atrophy. In three cases there were secondary carcinomatous growths in the suprarenals; bilateral in one case, unilateral in the other two. In one additional case there was a secondary nodule of carcinoma blocking the right suprarenal vein and associated with hæmorrhage into the corresponding capsule, but there were no growths in either.

Addison took a characteristically broad view of the relation of the symptoms to the morbid lesions, and expressed himself to the effect that any morbid lesion of the suprarenals may produce the same result, and that the result depends not so much on the nature of the organic change as upon the interruption of some special function of those organs.

After the publication of his original memoir, Addison appears to have been inclined to modify his views in respect of the multiplicity of morbid conditions of the suprarenal capsules and the uniformity of the series of symptoms, and to have desired to remove from among the cases in his monograph those of malignant disease of the suprarenal capsules. With regard to the cause of the symptoms, he conjectured that the intimate connection of the suprarenal bodies with the sympathetic was largely concerned in their production; thus in some degree throwing over his original opinion that the interruption of some special function of the suprarenal capsules was the explanation of the characteristic features of the disease.

According to Sir S. Wilks (Guy's Hospital Reports, 1862), Addison at a discussion at the Royal Medical and Chirurgical Society expressed himself as follows:—"We know that these organs (the suprarenals) are situated in the direct vicinity and in contact with the solar plexus and semilunar ganglia, and receive from them a large supply of nerves, and who can tell what influence the contact of these diseased organs might have on these great nerve centres, and what share that secondary effect might have on the general health and in the production of the symptoms presented?"

Wilks taught, and with no uncertain voice, that all genuine cases of Addison's disease are due to one and the same lesion of the suprarenal bodies. This view might be called the unity of Addison's disease. The lesion would now be considered to be tuberculous, but Dr. Wilks considered it to be a primary inflammation comparable to hepatic cirrhosis, and regarded the atrophied cirrhotic condition of adrenal bodies, sometimes seen, as the last stage of the fibro-caseous change.

Dr. Greenhow was a follower of the doctrine of the unity of Addison's disease, and therefore criticised severely all the recorded cases in which the morbid condition of the suprarenal bodies was other than the fibro-caseous change; and concluded either that the symptoms (especially the pigmentation) were not characteristic of Addison's disease, or that the lesion found was incorrectly described.

The conditions of the suprarenal bodies recorded in cases of Addison's disease are the following:—

(i.) The fibro-caseous lesion due to tuberculosis—far the commonest condition found.

(ii.) Simple atrophy, sometimes so extreme that the organs cannot be found after death.

(iii.) Chronic interstitial inflammation leading to atrophy.

(iv.) Malignant disease invading the capsules, including Addison's case of a malignant nodule compressing the suprarenal vein.

(v.) Blood extravasated into the suprarenal bodies.

(vi.) No lesion of the suprarenal bodies themselves, but lesions, pressure, or inflammation involving the semilunar ganglia.

The first is the only common cause of Addison's disease. The others, with the exception of simple atrophy, may be considered as very rare.

(i.) The fibro-caseous or tuberculous change in the suprarenal bodies begins in the medulla. It has been said to start in the cortex, but this must be exceptional. Care must be taken not to regard as small tuberculous masses the fatty adenomata which are frequently present on the surface of the cortex. Miliary tubercles, at first scattered in the substance of the medulla, increase in size, and, by coalescing, gradually replace the whole or varying amounts of the organs, which thus become enlarged—weighing several times the normal amount—nodular, and deformed. After destroying the cortex this morbid process readily sets up inflammation in the contiguous tissues, and is the cause of adhesions to the surrounding organs. When it is of old standing, fibrous tissue is developed around the caseous or mortar-like tuberculous masses, which from calcareous infiltration may become cretaceous. On the other hand, the caseous material may soften down so as to form an abscess in the enlarged suprarenal capsule.

Tubercle bacilli have been found very frequently; though, on the other hand, repeated and careful examinations may fail to demonstrate their presence. Delépine inoculated caseous material from the suprarenal bodies of a case of Addison's disease into guinea-pigs after Villemin's method, but no tuberculosis resulted. From this it may be concluded that, although the lesion is generally tuberculous, it is not necessarily so in all cases, or at least cannot be proved to be so.

Generally the lesion is present, though often in different stages, on both sides; but since its discoverer's time, cases of well-marked Addison's disease have been found associated with a unilateral lesion.

The fibro-caseous change is the one usually met with in Addison's disease. In 285 cases collected by Lewin it was present in 211 As in the lungs so in the suprarenal bodies, the tuberculous is more frequently seen than any other form of chronic inflammation.

Tuberculous change in the suprarenal bodies is frequently found without any signs or symptoms of Addison's disease, present or past Such cases should not be described as "Addison's disease without any symptoms"; for the affection is a clinical and not a pathological entity Of 131 cases in which death was chiefly or directly due to tubercle this was the case in 18. In 11 the lesion was unilateral, bilateral in the remainder. In contrasting the comparative liability of the suprarenal bodies to tuberculosis with the marked immunity of the thyroid gland it is noteworthy that the physiological actions of their respective extracts are opposed.

(ii.) Well-established examples of simple atrophy (43) of the suprarenal capsules, without any fibrous increase in the substance of the organ, or of any fibrous adhesions around them, have often been described as giving rise to the clinical picture of Addison's disease. The atrophy in some of the cases was extreme, the organs in many cases requiring very careful and minute dissection. In some instances they are described as being of the size of peas. It cannot be wondered at that in some cases, as in Dr. Spender's, they are described as being absent. These cases are of great importance, as will be seen later, in supporting the view that the symptoms of the disease are due to the absence of the functional activity of the organs, and not to irritation of the neighbouring important sympathetic nerves. In these cases of atrophy the sympathetic plexuses and semilunar ganglia were in most instances carefully examined, and stated to be normal.

(iii.) Chronic interstitial inflammation of the suprarenal bodies, leading to atrophy, and homologous with atrophic cirrhosis of the liver, has given rise to typical Addison's disease. The fibrosis is quite unconnected with the production of any caseous material, and does not show any evidence of tubercle, such as bacilli. The late Dr. Haddon (20) compared this change in the suprarenal bodies to those met with in the thyroid gland in myxœdema, and expressed his opinion that the essential factor in Addison's disease is, as in myxœdema, a destructive change, the anatomical condition being of no consequence as long as it is destructive.

(iv.) Malignant disease of the suprarenal capsules occasionally gives rise to some of the symptoms of Addison's disease; such as gastric disturbance, extreme debility, and pigmentation. Characteristic cases of Addison's disease are naturally those in which there is no other organ affected, and in which the disease runs its own course without any complications. When growths develop secondarily in the suprarenal bodies the primary growth may give rise to symptoms which throw into the shade or obscure any that may be due to interference with the suprarenal bodies. The comparatively rapid progress of the primary malignant disease may kill the patient before the secondary affection of the suprarenal bodies has had time to lead to any distinct symptoms. Again, in many cases the presence of malignant disease, if ascertained, would be quite sufficient to explain any symptoms which otherwise might be due to suprarenal disease. Still, from Addison's time downwards, examples of secondary malignant growths in the suprarenal capsules associated with the symptoms, especially with the pigmentation, of Addison's disease have been recorded; and it is to be borne in mind, therefore, that new growth in the suprarenal bodies may produce symptoms comparable to those met with in definite cases of Addison's disease.

It is undoubtedly true that the suprarenal bodies may apparently be almost completely destroyed by carcinoma, and yet no special symptoms result. The same, however, is true of tubercle, and especially where there is extensive tuberculous disease elsewhere. Perhaps in both cases death occurred before symptoms characteristic of Addison's disease have had time to develop.

In primary malignant disease of the suprarenal bodies there seems little evidence that the symptoms of Addison's disease occur.

(v.) A few cases have been recorded, showing an apparent connection between hæmorrhages into the suprarenals and blood-cysts occupying them, on the one hand, and the symptoms of Addison's disease on the other.

(vi.) Definite lesions of the suprarenal bodies are present in about 88 per cent of the cases of Addison's disease (23). Apart from disease of the suprarenals of the various kinds already mentioned, there are cases in which symptoms like those met with in Addison's disease are found in association with alteration of the semilunar ganglia or abdominal sympathetic; the suprarenal bodies appearing healthy. Thus the solar plexus and semilunar ganglia have been surrounded by lymphadenomatous growths, while the suprarenal bodies were found to be intact. In such instances there must be considerable interference with the vascular connections of the suprarenal bodies, more especially with the thin-walled veins or lymphatics.

Condition of the adjacent sympathetic, etc.—The condition of the semilunar ganglia and sympathetic plexuses has been the subject of much attention. They have been found invaded by the inflammatory process, sclerosed, and degenerated.

Dr. Greenhow described two stages in the process: (*a*) a stage of irritation of the semilunar ganglia and the nerves connecting them with the suprarenal capsules, as shown by redness and swelling; and (*b*) a further stage of atrophy and fatty degeneration.

On the other hand, the absence of any alteration of these same structures has been repeatedly recorded. Thus 49 cases of Addison's disease due to tuberculous disease of the suprarenal bodies, in all of which the condition of the sympathetic was specially examined, were collected from various sources by Alexais and Arnaud. In at least 12—that is, 24 per cent—of these cases the nervous structures were described as normal. An intimate knowledge of the normal anatomy of the parts is of great importance. The extremely careful examinations made by Dr. Robinson for Dr. Mann (32) on two cases of Addison's disease serve as a model for such investigations; since a control examination was made at the same time of the same structures from a patient of the same age in whom there was no reason to suspect anything abnormal.

Von Kahlden has described hyaline degeneration and thickening of the vessel walls, small-cell infiltration, and hæmorrhages in connection with their adventitia, and pigmentary atrophy of the ganglion cells and thickening of their capsules. He considers that these changes have a direct causal relation to the symptoms of Addison's disease. He found the splanchnic nerves in the two cases quite healthy. Jurgens and Fleiner, however, have described degeneration of the splanchnics in Addison's disease. The bearing of these observations must be considered in the light of Hale White's description of the normal histology of the semilunar ganglia in adults. The cells are pigmented and atrophied, the degree of atrophy increasing with age; the fibrous tissue was often very much increased in amount, and in a few instances the section was crowded with leucocytes without any apparent reason.

The condition of the semilunar ganglia and of the adjacent sympathetic being so inconstant in cases of disease, the changes described in them have no satisfactory claim to be considered as causal factors in the production of the disease.

Changes in the central nervous system have been described in a few cases only, and, if they had any relation at all to the disease, were the result rather than the cause of the morbid state. A softened condition of the brain, with an increased amount of cerebro-spinal fluid, has been recorded in some cases of Addison's disease, and was probably accidental; but its occurrence is of interest from the marked inflammatory changes resulting from removal of the suprarenal bodies in animals in Tizzoni's hands. Tizzoni quotes two cases of Addison's disease in which lesions of the central nervous system were found: 1. Bourredi's case: Caseous change in the suprarenal bodies associated with hyperæmia of the cord, perivascular inflammation, degeneration of nerve fibres, and changes of varying degree in the ganglion cells. 2. Semmola's case: A normal condition of the suprarenal capsules, accompanied by mucoid degeneration of the stroma of the abdominal ganglia of the sympathetic, and small-cell infiltration around the central canal of the spinal cord.

In connection with the view that Addison's disease is of the nature of a toxæmia, it would be natural to expect to find changes corresponding to those described recently in the spinal cord in pernicious anæmia.

Neuritis of the posterior root ganglion and sclerosis of the cord have been described in some cases, but further observations are required.

Other anatomical lesions.—Hypertrophy of the lymphoid follicles of the stomach and intestines, enlargement and softening of the spleen, and occasionally persistence of the thymus, may occur. Dr Greenhow spoke of the prominence of the lymphoid follicles of the intestinal tract as one of the characteristic, though perhaps not quite invariable lesions of the disease.

Pigmentation of the peritoneum has been recorded in a few isolated instances, but is probably the result of inflammation, and not therefore of any special importance. Similar change is not met with in other serous membranes. Pigmentation of the pia mater (24) has once been observed; but here again it may possibly have been due to some accidental or concomitant cause, such as the melanæmia of ague.

Pigmentation of the peritoneum and mucous membrane of the intestine occurred in a case of Addison's disease under Dr. Allchin (7); there were old peritoneal adhesions, but the specimen is quite free from any ulceration.

Anatomical distribution of cutaneous pigment in Addison's disease.—Microscopically the pigment is found in the cells of the stratum Malpighii, the more superficial layers of the epidermis being quite or almost free from any pigment.

The dermis shows a few pigmented cells, "carrier cells," which, it is thought, convey the pigment from the blood-vessels of the dermis to the stratum Malpighii. These wandering cells are found around the vessels in the superficial parts of the dermis, where they absorb pigment from the blood-vessels, the mode of absorption being doubtful. That hæmoglobin is not absorbed directly is shown by the absence of iron from the pigment of the skin, both in normal conditions and in Addison's disease. If eventually the pigmentation of normal skin is derived from the blood pigment, very considerable metabolism must intervene. Possibly the skin pigment is not derived from that of the blood, but is manufactured by the activity of the cells of the tissue, which itself depends on the supply of lymph. This supply of nutrient lymph would in its turn vary with the conditions of the neighbouring vessels.

Further, it has been suggested that the pigmentation of Addison's disease is due to an increased formation of pigment in the stratum Malpighii depending on excessive or altered nervous stimulation; but it is evident that it is extremely difficult to eliminate vascular changes as a factor in pigmentation, since in all probability increased nervous stimulation and increased functional activity of the skin would both be accompanied by vascular dilatation. The existence of special nerves influencing pigmentation, through their action on cells like chromatoblasts, has not yet been proved.

The view that the pigmentation is due to an increased supply of blood pigment passing into the skin as a result of functional or organic changes in the vessel walls is perhaps that generally accepted.

Situation of the pigment on the mucous membrane.—According to Dr. Greenhow, the pigment in the tongue is found in the same layer as in the skin; namely, the stratum Malpighii or mucosum. Haddon found the pigment quite as plentiful in the corium as in the stratum mucosum of the buccal mucous membrane. Tizzoni, in the pigmentation produced experimentally in the buccal mucosa of rabbits, found pigmented carrier cells in the corium, and pigment in the deeper layers of the stratum mucosum.

Dr. Dixon Mann draws a sharp distinction between pigmentation of the mucous membrane and that of the skin. Pigmentation of mucous membranes is not general; it requires certain local conditions (friction, local hyperæmia) for its development, and the pigment has a different histological site. The corium contains pigmented carrier cells, as is the case in the skin, but the stratum mucosum contains no pigment, possibly because the cells composing it do not have the finger-like processes which in the skin are thought to receive the pigment from the carrier cells. When, exceptionally, pigment was found in the stratum mucosum, it was seen to be not in but between the cells.

PATHOLOGY.—The association between the morbid lesions on the adrenals and the characteristic symptoms of Addison's disease has given rise to much discussion. There are two distinct theories which require consideration.

The nervous theory of Addison's disease.—The early experimental work of Phillipeaux, Harley, and, more recently, of Tizzoni, pointed to the absence or unimportance of any function on the part of the suprarenal bodies. This negative view of the functions of the suprarenal bodies held the field from Addison's discovery until quite recent times On such a physiological basis the connection between disease of the suprarenal capsules and Addison's disease was explained by the secondary morbid changes, induced by the lesions of the suprarenal bodies, in the neighbouring semilunar ganglia, solar plexus, and sympathetic nerves This conception will be for ever associated with the name of Sir Samuel Wilks. It was based on post-mortem investigation, showing the spread of inflammation from the tuberculous suprarenal bodies to the semilunar ganglia and other branches of the sympathetic.

Dr. Greenhow inferred that at least all the more important features and prominent symptoms of the disease were due to morbid changes in the nerves, the changes in the nerves being first of the nature of irritation and later of atrophy. The collapse and the extreme state of debility are thus explained as the result of the altered condition of the sympathetic in the abdomen. The vomiting and pigmentation are referred to the direct irritation of the sympathetic by the caseous material in the suprarenal bodies, or to the same cause acting reflexly through the cerebro-spinal system.

The view of Wilks and Greenhow may be summarised thus:—The lesion is primary in the suprarenal bodies, and always of the same nature; while the symptoms of the disease are due to the secondary effect on the adjacent sympathetic, the solar plexus, and the semilunar ganglia. Arnaud and Alexais accepted the principle, but, by limiting the nervous changes to the ganglia in the fibrous capsule of the adrenal bodies, they were able to explain the fact that in Addison's disease the solar plexus and semilunar ganglia may be healthy.

A natural modification of these views is that Addison's disease is due to changes in the abdominal ganglia and sympathetic, which may be due to disease of the suprarenal bodies, but are independent of a special, or indeed of any lesion in them. This theory was supported by Jaccoud, von Kahlden, and others, from the clinical and morbid anatomy points of view, and by the experimental researches of Tizzoni. It has been suggested that the irritation of and subsequent changes in the ganglion cells and sympathetic fibres enclosed in the fibrous capsule of the suprarenal bodies give rise to the symptoms of Addison's disease (6). In this way the nervous theory of Addison's disease can be upheld even in cases where the semilunar ganglia and abdominal sympathetic are not found to have undergone any abnormal change. The comparative rarity of these ganglion cells in the capsule of the organ renders this view unlikely, and in any case it would not explain the symptoms when the capsules are merely atrophied. The unimportance of the part played by the suprarenal bodies themselves was carried to an extreme by Semmola. He believed that not only had changes in the suprarenal bodies nothing to do with Addison's disease, but that also when they did exist, they were trophic lesions due to disease of the nerves which presided over their nutrition.

The nervous theory does not explain the numerous cases recorded of typical Addison's disease, in which special attention has been paid to the condition of the semilunar ganglia and adjacent sympathetic, and in which they have been found to be normal; since continued irritation could not last for any time without setting up local inflammatory changes. Still less does it explain the occurrence of the symptoms of Addison's disease associated with simple atrophy of the adrenal bodies.

Conversely, there are numerous examples of slow irritation of the abdominal sympathetic by enlarged glands, spinal caries, surgical and tuberculous kidney, abdominal aneurysm, and chronic peritonitis, where no symptoms of Addison's disease appeared, except, perhaps, some pigmentation.

Experimental cutting of all the nervous connections of the suprarenal body does not give rise to the symptoms, produced either by its removal or by ligature of its efferent vein (Thiroloix), which are somewhat analogous to those of Addison's disease in man. Experimental removal of the cœliac plexus leads to rapid emaciation, low temperature, diminution in the amount of the urea in the urine, acetonuria (though this is disputed), and acetonæmic coma. These results do not support the view that Addison's disease is due simply and solely to an irritating and destructive lesion of the sympathetic around the suprarenal bodies. As has been already seen, the nervous theory is untenable, at any rate in any exclusive sense, for the sympathetic in the neighbourhood of the suprarenal bodies is not constantly altered.

The theory of suprarenal inadequacy.—If the purely nervous theory of Addison's disease cannot be reconciled with the facts, attention must be directed to Addison's first and original view, that the symptoms of the disease are due to interference with the functional activity of the suprarenal bodies. This is to say in other words that Addison's disease is the outcome of suprarenal inadequacy. Before considering the functional activity of the suprarenal bodies it will be well to clear the ground by inquiring whether the facts of morbid anatomy are consistent with the hypothesis that Addison's disease is due to interference with or loss of function of the suprarenal bodies.

Bearings of morbid anatomy on the theory of adrenal inadequacy.—It is known that destructive tuberculous lesions and atrophy of the suprarenal bodies may give rise to the symptoms of Addison's disease.

But the following objections may be raised to the theory of suprarenal inadequacy:—

(*a*) The existence of cases where after death the suprarenal bodies are found to be extensively destroyed by tubercle or new growth, and in which, nevertheless, definite clinical symptoms of Addison's disease have been absent during life. (*b*) That there are cases, clinically of Addison's disease, in which post-mortem caseation of comparatively small amount is found in the suprarenal capsules—perhaps only in one, and in which the amount of damage is even less than in cases which have presented no sign of Addison's disease. Since a comparatively small part of the available suprarenal substance is thus rendered functionless, it has been argued that the concomitant symptoms cannot be due to abolition of the function of the organs. And (*c*), lastly, that there are examples of Addison's disease in which the suprarenal capsules themselves are healthy, though the surrounding sympathetic nerve plexuses and semilunar ganglia are involved in dense adhesions or in a growth, such as lymphadenoma.

In reply to these objections the following considerations may be brought forward:—

(*a*) In cases where the organs are extensively destroyed by tubercle, or invaded by new growth, the absence of symptoms may be explained in two ways: (α) the change in the adrenal bodies is usually a secondary result of advanced disease in other organs, which kills the patient before the symptoms of Addison's disease, usually a chronic affection, have time to develop. (β) That some compensation for the destruction of the suprarenal glands is present in accessory suprarenal bodies, and that, as in the case of the thyroid gland, symptoms due to the destruction of the main glands are thus avoided.

(*b*) In reply to the objection that when the lesion of the suprarenal substance is not of considerable amount the remaining part of the organ, if healthy, should produce compensation, and thus prevent the development of symptoms, it may be urged that failure in this power of compensation may be due to inherent want of vitality, to concomitant atrophy, or possibly—and this is a point requiring investigation—to an interference with the efferent vessels by the tuberculous growth. The common tuberculous caseous change always begins in the medulla, and thus might easily obstruct the vascular and lymphatic connections of the organ, and so render it impotent, even though a sufficiency of secreting gland tissue were left. For it should be noted that the medulla is the part of the organ which provides the active secretion, the function of the cortex not being yet known.

(*c*) In the few cases of Addison's disease, where the suprarenal bodies are described as healthy, while the sympathetic and semilunar ganglia were involved in dense adhesions or in a growth, it is possible that the vessels and lymphatics of the suprarenal capsules were thus interfered with, and so the organs were practically placed outside the circulation and rendered functionless. The sequence of events, then, may be compared to Boinet's experimental ligature of the pedicle (and veins) of the suprarenal bodies, with its resulting fatal toxic effects. Hence it may be concluded that obstruction to the efferent vessels of the suprarenal capsules is a possible cause of Addison's disease. The facts of morbid anatomy, then, appear to be compatible with the view that Addison's disease can be explained by suprarenal inadequacy.

Physiology of the suprarenal bodies.—Brown-Sequard (10) showed in 1856-1858 that the suprarenal bodies are necessary to life, and that when deprived of them animals die rapidly. This observation has been amply confirmed by subsequent observers. In cases where their removal has not led to a fatal result, it is probable either that the glands were not entirely removed, or that accessory suprarenal bodies were present, which, as Stilling has shown, are capable of undergoing compensatory hypertrophy.

As the result of all modern work, it is clear that the suprarenal bodies are active functional glands. This is not the place to describe in detail the physiology of suprarenal glands; for this the reader is referred elsewhere (21) (43) (45): but two conclusions as to the function of the glands are possible as the outcome of this work. (A.) That the suprarenal bodies are excretory or katabolic in function: that they pick up and remove from the circulation effete blood pigment and toxic bodies, and destroy them. (B.) That these organs are secretory or anabolic: that they manufacture some fluid, an internal secretion which passes into the blood-vessels or lymphatics, and is of use in the economy.

Addison's disease, then, is either an auto-intoxication due to the deficient excretory activity of the suprarenal capsules, or the result of an inadequate internal secretion on their part.

A. *That Addison's disease is an auto-intoxication due to inadequate excretory activity of the suprarenal bodies.*—Of this first alternative there is no proof. Dr. MacMunn (30) believes that, normally, hæmoglobin and histohæmatins become changed into hæmochromogen in the suprarenal bodies. Hæmochromogen, according to him, is blood pigment in an excretory stage and is found also in the bile. He holds that in Addison's disease the failure of this function of the suprarenal bodies is shown by the presence of a pigment—urohæmatoporphyrin—in the urine. This body, which MacMunn also found in various other conditions, has been shown not to be a definite chemical body, but to be a mixture of a larger quantity of hæmatoporphyrin and a smaller quantity of urobilin (15), both of which are among the normal urinary pigments. It has also been shown that the urinary pigments are not increased in Addison's disease, and that hæmatoporphyrin may only be present as a trace (16). It is highly improbable, therefore, that the suprarenal bodies have any action on the effete blood pigments.

What evidence is there that the suprarenal bodies remove toxic substances from the circulation and then destroy them? Large doses of suprarenal extract certainly kill animals, and Abelous and Langlois find that if the suprarenal bodies are removed from an animal the blood becomes toxic to other animals, of the same species, the suprarenal capsules of which have been removed, the transfused animals dying sooner than they otherwise would. Blood from a few control animals, dying from other causes, did not appear to possess this toxic effect; but more observations are required as to the question whether the blood of dying animals is toxic or atoxic. It is conceivable that this toxæmic condition was the result of a suspension of the excretion of poisonous bodies by removal of the suprarenal capsules. But Tizzoni and Nothnagel crushed the suprarenals, and left them to be absorbed without any resulting signs of toxæmia; so that, at any rate, the suprarenal bodies do not contain the poisonous substances which they might be supposed to remove. This same hypothesis is further opposed by the experiments of Abelous and Langlois, who showed that the toxæmia due to ablation of the organs can be counteracted by injection of suprarenal extract. Now, if the suprarenal bodies excrete a poison which, when accumulating in the blood, gives rise to toxic symptoms, injection of suprarenal extract should increase these toxic effects.

These two observations, then, are both opposed to the hypothesis that the suprarenal bodies excrete a poisonous substance. On the other hand, it is known that injection of very large quantities of suprarenal extract, equal to several times the weight of the suprarenal bodies, produces death. Now this at first sight might seem to tend in the opposite direction, but it does not really do so. It only proves that an abnormal and poisonous dose of suprarenal extract or secretion has been used.

Again, Abelous and Langlois showed that after removal of the suprarenal bodies a toxic body, with properties like curare, appears in the blood. But, on the other hand, Schäfer and Oliver (45) found that the effect of suprarenal extract was not at all comparable to that of curare. These two experiments are not contradictory: they only show that the body or bodies extracted from the suprarenal capsules are not the same as those present in the blood of animals whose adrenals have been removed. This is a strong argument against the hypothesis that the suprarenal bodies are excretory glands.

There is, then, no satisfactory evidence that the suprarenal bodies remove effete blood pigment from the blood, or absorb toxic bodies and render them harmless.

B. *That Addison's disease is due to an inadequate secretion on the part of the suprarenal bodies.*—Since the function of the suprarenal bodies is not excretory we are left with the alternative view that they are secretory glands providing an internal secretion like the thyroid. The researches of Abelous and Langlois and of Schäfer and Oliver form the basis for this belief.

Abelous and Langlois come to the conclusion that the internal secretion normally antagonises or renders harmless toxic bodies formed by the general metabolism, but especially in the muscles of the body. On removal of the suprarenal bodies these toxic substances accumulate in the body and give rise to an auto-intoxication. They compare the action of these poisonous substances to that of curare. In the light of these views Addison's disease might again be regarded as an auto-intoxication which, except in the way in which it is produced, is the same as that which would result from an accumulation of poisons not excreted.

Schafer and Oliver have shown that the medulla of the suprarenal bodies yields a substance possessed of marked physiological properties: it increases the tone of muscular tissue generally, and especially of the heart and arteries. Removal of the suprarenal bodies leads to extreme muscular weakness and loss of tone in the vascular system. On these data Addison's disease is a condition of general atony and apathy due to absence of the internal secretion of the suprarenal bodies, which nominally keeps up the vascular and muscular tone of the body.

To recapitulate. The nervous hypothesis of Addison's disease as an exclusive explanation of the symptoms has already been shown to be untenable. The two remaining hypotheses are—

(i.) That it is an auto-intoxication due either (*a*) to imperfect excretion on the part of the suprarenal bodies—the objections to this view have already been stated at length; or (*b*) to a deficient internal secretion on the part of these glands.

(ii.) That it is merely a condition of atony due to an absence or deficiency of the normal internal secretion.

The two hypotheses which are based on an inadequate internal secretion of the glands will now be stated.

That Addison's disease is an auto-intoxication.—Since there is no evidence that the suprarenal bodies are excretory, this theory implies that as a result of a deficient internal secretion a toxæmic condition results.

It is conceivable that the internal secretion might normally antagonise toxins resulting from the metabolism of the body generally in several ways—(*a*) In a manner analogous to the neutralisation of an acid by an alkali; of this there is no proof. (*b*) By exerting a ferment-like action on these hypothetical toxins and destroying them. Schäfer and Oliver's researches are, however, opposed to the view that the active principle of the internal secretion is a ferment, so this hypothesis falls to the ground. (*c*) By regulating the metabolism of the tissues, and preventing their running riot and producing abnormal or toxic bodies (*d*) By increasing the resistance and defensive powers of the cells of the body, including the white blood corpuscles, so that they are able to withstand the poisonous bodies possibly resulting from the general metabolism of the body, and to destroy them.

Of the two latter views there is no proof in either direction. The symptoms of Addison's disease are so far analogous to those of diseases due to a toxic condition of the blood, such as uræmia and pernicious anæmia, as to suggest that the disease is a toxæmia.

The extreme debility may be considered either as a result of a toxic condition, or as a state of atony due to the absence of a necessary stimulus. The vomiting, gastro-intestinal disturbances, and pigmentation point rather to some positive irritation than to a mere absence of a normal stimulus.

The experimental basis for the opinion that Addison's disease is an auto-intoxication consists partly in the observation that, after the removal of their suprarenal capsules, animals die with symptoms resembling curare poisoning (Abelous and Langlois). It has been shown, however, that the motor nerve endings are not paralysed even up to the time of death (18). The auto-intoxication theory has been supported on the ground that the blood of animals from which the suprarenal capsules have been removed is toxic for other animals who have undergone the same operation, hastening their death; while blood from an animal dying from a different cause did not accelerate the fatal termination. Schäfer (44), however, has pointed out that it is probable that the blood of any animal dying slowly becomes toxic, and that acapsuled animals would be especially susceptible to it. Until we have further evidence on this point it is not satisfactorily proved that the blood of acapsuled animals becomes specifically toxic.

If Addison's disease is an auto-intoxication the urine should contain the toxic material, since the kidneys are practically always healthy, and are not, as in uræmia, incapable of performing their excretory function properly. Here a sufficient amount of evidence is unfortunately wanting. Schäfer and Oliver have found that extracts from the urine of patients suffering from Addison's disease have the same effect as normal urine Geoffredi and Tinno have found the toxic coefficient of the urine increased, but this was in a case where there was in addition caseous tuberculous pneumonia; so that no real importance can be attached to this observation. Neurin has been said to be present in the urine, and the phenomena of the disease have been referred to its action (33). This statement especially is in need of more general confirmation. More recently Mühlmann has put forward the view that the symptoms of Addison's disease are due to chronic poisoning with pyrocatechin. More extended observations are required, and until they are forthcoming judgment must be suspended. That Addison's disease is an auto-intoxication is no doubt an attractive supposition, but as yet there is but little positive evidence to support it.

That Addison's disease is a condition of atony due to absence of the stimulating effect of the internal secretion of the suprarenal glands.—Schäfer and Oliver have shown that the medulla of the suprarenal bodies provides an internal secretion which exerts a marked tonic effect on the muscular system, especially on the heart and blood-vessels; while removal of the suprarenal bodies leads, as might be expected, to an extreme condition of want of muscular tone. They also found that the suprarenal capsules in Addison's disease did not contain any of this active principle. From these data it appears probable that Addison's disease is a condition of debility due to an absence of the internal secretion normally supplied by the suprarenal bodies.

It should be remembered, however, that we are as yet far from a full understanding of the method of action of internal secretions. The secretion of the suprarenal bodies, by its interaction with other glands, might produce the equilibrium we know as health. Absence, deficiency, or perversion of the suprarenal secretion appears to lead to a profound disturbance of normal processes in the body. This disturbance might easily lead to the production or accumulation of poisons in the system—in other words, to an auto-intoxication. The problem is a complex one, and at present the data for solving it are wanting.

To sum up. Addison's disease is due to an inadequate supply of suprarenal secretion. But whether the deficiency in this internal secretion leads to a toxic condition of the blood, or to a general atony and apathy, is a question which must remain open. It should be added that Byrom Bramwell and Boinet have recently argued in favour of Addison's disease being due partly to direct irritation and neuritis of the sympathetic and partly to suprarenal inadequacy. According to this view, the nervous and insufficiency theories are combined, and neither is exclusively right or wrong.

Onset.—The onset of the disease is generally insidious and not marked by any special symptoms or features. The patient has been gradually losing energy and strength for a considerable time before seeking medical advice, which he does perhaps chiefly for the relief of gastric symptoms. Pigmentation may occasionally precede the manifestations of constitutional symptoms, and so be the first thing to be noticed; but the constitutional symptoms of general debility and gastro-intestinal irritability usually precede it.

In a few cases the rapid occurrence of severe symptoms may suggest a sudden onset; it is probable, however, that this is rather a well-marked exacerbation in the course of this insidious disease than absolutely its first manifestations. The apparently acute onset of Addison's disease has been known to follow some sudden shock or depressing circumstance, and has been put down to the administration of a severe purge or to distress or worry.

Symptoms.—*Pigmentation* is the symptom which most often arouses the suspicion of the disease. Unfortunately it is variable both in the time of its appearance and in its degree.

Usually it follows the constitutional symptoms, and it may only occur shortly before the fatal termination, and be then but slightly marked or even entirely absent. In some infrequent instances the pigmentation appears to precede any subjective symptoms by years. In a case of Dr. Munro's, quoted by Dr. Greenhow, there was an interval of seven years between the appearance of pigmentation and the onset of constitutional symptoms. In some cases it is so marked as to resemble that seen in the dark races; such cases are, however, rare: more often it resembles the bronzing of sunburn, or the dirty sallow tint so frequently seen in association with dyspepsia: the patient himself is often quite unaware of its presence. It may attract little notice even on the part of the patient's friends, who are generally the first to observe it; or it may be put down by them to exposure, or to insufficient attention to personal cleanliness.

The pigmentation is an exaggeration of the normal, it has, generally speaking, the same regional and anatomical distribution, and is subject to the same influences, being increased by any local irritant applied to the skin.

Hilton Fagge (25) thinks it probable that it would be absent in a patient kept in the dark. This experiment, so far as I know, has not been intentionally tested; but the light to which patients are exposed may very well play a part in determining pigmentation at an early or a late stage of the disease.

It would be interesting to know whether Addison's disease has ever been observed in an albino. The probabilities are against the concurrence of two such rare conditions; but, theoretically, there should be no pigmentation in such a case.

Pigmentation is sometimes almost universal, but is usually partial, and is then first noticed on the face, neck, and the backs of the hands and fingers; especially over the joints, where it throws into relief the nails, which appear remarkably white: in this last point the pigmentation of Addison's disease differs from that of the dark races, which it otherwise closely resembles.

The tint of the face is of very varying intensity, and contrasts with the sclerotics, which usually appear somewhat anæmic. In rare instances the conjunctivæ show foci of intense pigmentation.

The staining of the neck and face, like that seen occasionally in pregnant women, may show considerable irregularity in its degree. There may be darkening of the hair during the progress of the disease, but according to Wilks (57) the colour of the hairy scalp is not altered;

and the same is true of the skin where it is covered by the beard, etc., and of the eyelids.

The lips, along the line where they come in contact, may in some instances show pigmentation; and similarly, as the result of irritation most commonly due to carious teeth, the cheeks, the gums, or the tongue may become pigmented. Pigmentation of mucous surfaces is often absent, and though it is generally regarded as a sign of considerable value, it is probable that the factor of local irritation is a powerful one in its development.

Should pigmentation of the mucous membrane of the mouth be found without any source of irritation, it may perhaps be regarded as an exaggeration of some trace of the condition seen in Lascars, in blue-gummed Negroes, and, exceptionally, in healthy persons (39). A similar example of pathological reversion to a past type is seen in the occasional occurrence of melanotic sarcoma of the palate, or is more nearly paralleled by a case, recorded by Dr. Mott (34), of a melanotic tumour of the lip.

The tongue may show purplish inky stains near the free border, stains so arranged as to suggest contact with the teeth as a causal factor.

Passing from the exposed parts of the body, the pigmentation is found on the dorsal surface of the forearms and on the anterior folds of the axillæ; these, it should be remembered, are apt normally to show pigmentation.

The areolæ around the nipples show a marked alteration in tint, comparable to that seen in pregnancy; but of course the glandular activity and development of the mammary veins are absent.

The lower part of the linea alba may belie its name, and become a dingy or brown streak.

The genitals and groins are darkened in tint, sometimes to a marked degree. It is said that the mucous membrane of the labia minora and vagina may present changes similar to those seen in the mouth.

The dark areas pass by a gradual transition into the paler parts of the skin; the pigmented regions have no sharp margins. If, however, any part of the cutaneous surface have been irritated, as for example by a blister, the resulting increase in pigmentation has a comparatively sharp definition. Parts of the body which are exposed to friction or pressure show an increased pigmentation in an especial degree. Thus the waist where it is compressed by corset or belt, the knee where the garters are tied, the shoulders under the braces, or the prominent vertebral spines, present a darker hue. The palms of the hands and the soles of the feet, which are subject to as much if not more pressure than other parts, are very rarely pigmented.

The tissue of scars remains unaffected, but the surrounding skin shows an exaggeration of pigmentation. Dr. B. Bramwell has reported a case in which the pock-marks of variola were pigmented.

Dr. Greenhow attached considerable diagnostic value to the presence of small, well-defined specks, like small moles, on already discoloured parts of the skin. Dr. S. West has recently recorded a case in a woman which, in 1891, was diagnosed as Addison's disease. She then presented these pigment spots; four years later she came under treatment for anæmia secondary to menorrhagia; the skin was sallow, almost bronzed, but the pigment spots had disappeared. The patient may have had Addison's disease, for cases of longer duration, even lasting for ten years, have been recorded. It may, however, be questioned whether these spots should be considered pathognomonic of the disease.

Generally speaking, pigmentation, though suggesting the disease, is not of itself, apart from constitutional symptoms, sufficient to warrant a positive diagnosis.

The presence of pigment in parts of the body not available for clinical observation, and its histological relations in the tissues, are referred to under the heading of morbid anatomy.

Asthenia.—This is perhaps the most frequent and important of the constitutional symptoms. At first the patient is easily tired, never feels rested, even after a long night, and gradually becomes more and more indisposed for any exertion, however slight, whether of body or mind. As the disease advances, life becomes a burden, but the sufferer has not even sufficient vitality to complain of its weight. Impotence is seldom referred to in the reported cases, but is probably not infrequently present. The muscular feebleness is not accompanied by any corresponding emaciation; there are no signs of peripheral neuritis. This condition of invincible languor has been compared to that brought about by the action of a poison like curare in a minor degree.

Langlois (27) lays stress on the total loss of sustained muscular effort which distinguishes Addison's disease from phthisis and other causes of great debility. In fact, in cases of doubtful diagnosis he recommends recourse to Mosso's ergograph.

Symptoms referable to the vascular system.—The want of muscular tone and contractility is not limited to the voluntary muscles. The systole of the heart is greatly enfeebled, as is shown by the small, extremely soft and compressible pulse which, in some cases, may even become imperceptible at the wrist.

The temperature is generally subnormal and the extremities cold, so that the patient's state has been compared to that of chronic collapse. The depressed state of the circulation is further seen in a tendency to syncope; especially when the patient's head is raised. There is considerable danger that one of these fainting fits may prove fatal.

Cardiac weakness is also sometimes shown by palpitation and distressed breathing on movement. Sighing and yawning are sometimes present. An offensive or cadaveric smell is occasionally noticed to emanate from the patient

Although the temperature is usually below normal this is by no means universal; MacMunn and others have drawn attention to the association of Addison's disease with fever, which, however, may not appear till shortly before death.

Addison, probably from the fact that he discovered this disease when looking for the cause of pernicious anæmia, considered anæmia as one of the chief symptoms. Wilks (57), however, expressly states that neither the clinical features nor the post-mortem appearances are those of anæmia; and Osler (40) says that the blood count is usually 50 to 60 per cent of the normal. It is true that the contrast of the bronzed skin with the sclerotics, which are usually pearly, may give the impression of anæmia. But though anæmia and Addison's disease may coincide, they are not especially, much less inseparably, connected.

The subjects of Addison's disease retain about as much subcutaneous fat as they had before the onset of the disease. They may be thin or spare and lose weight, but they do not become remarkably emaciated.

Gastro-intestinal symptoms.—The tongue is usually clean and moist, but the appetite is poor and may be capricious. The loss of the healthy desire for food is an early symptom, and accompanies the insidious onset of general debility and loss of tone. In the later stages this indifference may pass into positive loathing. Nausea and retching are generally met with. Vomiting may occur throughout the course of the illness, but "is rarely absent in advanced stages, and may be spontaneous, and so irrepressible as to cause death from exhaustion" (Greenhow). Persistent hiccup may be a troublesome feature.

The bowels are usually confined, but severe attacks of diarrhœa may supervene, and are sometimes so uncontrollable as to carry the patient off. The constipation is but one more manifestation of the general loss of muscular tone already referred to.

Nervous symptoms.—The general loss of vitality is shown by the depressed functional activity of the nervous system. The acuity of vision may be impaired, flashes of light may pass before the eyes, and the perception of auditory sensations is sometimes dulled. The mental processes remain clear to the end, or until a final coma or delirium supervene. In such a condition of unconsciousness signs of irritation of the nervous system may show themselves in muscular twitchings or rigidity, or even in general convulsions. Headache and vertigo are by no means rare, and are most often associated with faintness. Pain is sometimes complained of in the limbs, and is often present in the loins, epigastrium, or hypochondriac regions. The extension of inflammation from the adrenal bodies to the neighbouring organs and tissues is probably responsible for much of the lumbar pain.

Urine.—There are no constant or characteristic features in the urine. It is usually normal, or slightly diminished in amount, though there may be polyuria. Albumin and sugar are absent. As an occasional result of intestinal disturbance indican may be present in the urine, but is not of any further significance.

MacMunn described a pigment, urohæmatoporphyrin, as being present in the urine; this body, however, is not a definite chemical compound, but is a mixture of a large quantity of hæmatoporphyrin with a smaller quantity of urobilin, both of which are among the normal urinary pigments. The observations of Thudichum and Dixon Mann show that there is a diminution rather than an increase of the urinary pigments. Cordone has recently described a pigment in the urine of cases of Addison's disease with the same characters as the melanin of the skin and of melanotic sarcoma.

The excretion of urea, as might be anticipated from the depressed metabolic processes, is probably diminished.

Neurin has been described in the urine by observers (33) who believe the disease is due to an intoxication set up by this body, but this description requires further confirmation.

Course of the disease.—The course of the disease is not uniform, and though progressive is not regularly so, even in the same individual. As in pernicious anæmia, there are exacerbations or paroxysms, during which all the symptoms become accentuated. After each of these crises the patient rallies, but is generally left in a worse position than before. Dr. Greenhow laid stress on these alternate exacerbations and remissions, and pointed out that the pigmentation follows the same lines, being exaggerated together with the symptoms; and that, though it diminished during the succeeding remission, it still remained more marked than it was before the last attack.

Usually the constitutional symptoms are the earliest to appear and the more prominent throughout.

Cases may prove fatal without any pigmentation; in these examples of Addison's disease without bronzing the symptoms usually run a rapid course. On the other hand, the pigmentation is occasionally the first, and for a varying time the only manifestation of disease. Sometimes one of the constitutional symptoms is more especially noticeable, sometimes another; thus there may be a tendency to vomiting and diarrhœa, the disease presenting a gastro-intestinal character; or fainting fits and extreme breathlessness on movement constitute what may be called a cardiac type. But all the while there is intense and increasing asthenia.

Duration.—The period over which symptoms referable to the disease occur is very variable. The onset is generally extremely gradual and the progress may be very slow; cases, indeed, have been recorded in which the duration appeared to be as long as seven or even ten years. Post-mortem the changes in the suprarenal capsules are as a rule of old standing—caseous or cretaceous tubercle. Whether after the development of definite symptoms the course of the disease can become arrested, and be considered cured, is a difficult question. The extremely prolonged course of some cases might well suggest that the morbid lesion had become arrested, and a certain degree of compensation effected; and that a recrudescence of tubercle, analogous to that often met with in the lungs, was responsible for the finally fatal issue.

There is no doubt that considerable destruction of the suprarenal bodies by tubercle is not infrequently met with in persons who have died from other causes, and in some of them the early symptoms of the disease may at some period, perhaps long antecedent to death, have been present; though possibly not sufficiently prominent to arrest attention. In any case of apparent recovery the difficulty of diagnosis and the possibility of the disease being latent must always be taken into consideration.

Be this as it may, the duration in the great majority of instances is long. The average length of time, in a number of cases collected by Wilks, during which symptoms were present was eighteen months. This calculation, however, included the rarer instances where the disease runs an apparently acute course. In the latter the lesion has been progressing, as seen at the autopsy, for months or even years, but no prominent symptoms had been manifested, and the disease has been spoken of as being latent. Suddenly, perhaps from some depressing conditions, the symptoms burst out in full force, and the patient dies in a few days or weeks. Between the very chronic and these remarkably acute cases there are intermediate grades which will be found to contain most of the cases met with in practice.

Termination.—Death may be quiet and gradual from asthenia, the patient being conscious to the last; or a "typhoid" or semi-comatose condition may precede it. Not infrequently sudden syncope extinguishes the flickering flame of life; this event, however, may occur long before the patient becomes bedridden; as in an instance recorded by Osler (38) of a physician who had hardly completed his arrangements for retiring from practice when he died from sudden syncope. Severe attacks of vomiting or diarrhœa may so exhaust the already debilitated patient as to be the immediate cause of death. Sometimes delirium, muscular twitching, or general convulsions may precede death.

Prognosis.—The disease when sufficiently advanced to warrant a positive diagnosis is probably always fatal. It must be admitted, however, that diagnosis in an early stage is not only difficult but uncertain. Its recognition by its features, when well marked, is much like the diagnosis of malignant disease by the cachexia, in which case it is equally true that the prognosis is hopeless.

As hinted in a preceding paragraph (Duration), it is quite conceivable that arrest may sometimes occur after initial symptoms of slight intensity have shown themselves. But though this is possible, it is difficult to prove. In 800 cases collected by Lewin, five cases are recorded as being cured, and twenty-eight as having shown improvement.

The bearing of treatment by suprarenal extract on prognosis will have to be considered in the light of a more extended experience. At present, though somewhat encouraging, it cannot be said that it bears any comparison with the effects of thyroid feeding in myxœdema.

Diagnosis.—The diagnosis of Addison's disease is by no means easy; we may suspect it, but to go farther and give a dogmatic opinion is often somewhat hazardous, and not warranted by the facts at our disposal.

Advanced and well-marked cases may be recognised at once; but the disease in its early stages, or cases in which either the pigmentation or the constitutional symptoms are absent or ill developed, may be regarded as the evidence of trivial ill health, or biliousness, or as merely accidental. Conversely minor ailments, especially the protean manifestations of dyspepsia, may simulate it. Although Addison's disease is sometimes revealed only on the post-mortem table, and this is especially so when the course is rapid and pigmentation is absent, it is probable on the whole, perhaps from the interest attaching to this comparatively rare affection, that it is more often diagnosed than proved to exist.

The diagnosis is rather one of exclusion, especially of abdominal disease, some forms of which may produce a passable imitation both of the pigmentation and of the constitutional symptoms of Addison's disease.

Since pigmentation is the most objective sign, and therefore the one which most frequently arouses a suspicion of Addison's disease, it will be well to consider first those conditions of pigmentation which may be mistaken for the melasma Addisonii. Chronic tuberculous peritonitis and malignant disease of the peritoneum, without apparently interfering with the functional activity of the suprarenal bodies, may be accompanied by considerable pigmentation of the face. The rare condition recently described as Acanthosis nigricans may supervene in cases of malignant disease within the abdomen. This pigmentation of the skin is most marked on the face, in the axillæ and groins; it differs from Addison's disease in the fact that the skin is thickened and shows an exaggeration of its normal folds. Acanthosis nigricans has been thought to be caused by pressure on the sympathetic. In some cases of malignant abdominal disease there may be compression of the vessels and lymphatics of the organ which is tantamount to rendering them functionless. The condition then is one of Addison's disease. A similar result has been met with occasionally in lymphadenoma involving the glands around the suprarenals. More rarely disease of the stomach may bring about darkening of the skin. I have recently had under my care a man with dilatation of the stomach, whose skin showed very considerable darkening which diminished as he improved.

Hepatic disease, and especially that rare condition, hypertrophic cirrhosis, associated with diabetes and pigmentation, or as Hanot, who first described this disease in 1882 with Chauffaud (22), now calls it, diabète bronzé, may produce very marked pigmentation of the skin. The after-effects of jaundice must be borne in mind in the diagnosis. Jaundice appears in former days not infrequently to have been confounded with the discoloration of Addison's disease; examination of the conjunctivæ and of the urine should at once settle any doubt.

Pancreatic disease, according to Fitz (13), may occasionally give rise to bronzing of the skin.

Pregnancy and uterine irritation in certain cases lead to very noticeable pigmentation of a somewhat patchy character.

To a slighter degree the skin may occasionally be affected in granular kidney.

In chronic phthisis pigmentation may be very considerable, but here, as in abdominal tuberculosis, it is chiefly found on the face.

Malarial melanæmia produces a general darkening of the skin, and in melanotic sarcoma marked pigmentation of the skin, quite apart from the presence of growths, has been noticed (29). According to Wagner, the histological position of the pigment in the skin in such cases of melanotic sarcoma is the same as in Addison's disease. Carbone considers that the presence of sulphur in the pigments of Addison's disease and of melanotic sarcoma distinguishes them from that resulting from the destruction of red blood corpuscles such as occurs in the melanæmia of malaria.

In exophthalmic goitre the skin may become so pigmented as to give rise to a diagnosis of Addison's disease combined with Graves' disease. Recovery in such a case may give rise to the erroneous impression that Addison's disease has been cured.

In chronic rheumatoid arthritis not only a darkening of the skin but the appearance of black freckles also may be noted. Occasionally in this disease a well-marked collar of pigment is seen on the neck.

Argyria is rare, but this discoloration, which follows on the absorption of silver salts and their subsequent deposit on the skin, is very striking. It is permanent, and has resulted from the medicinal use of nitrate of silver internally for nervous disease such as locomotor ataxia, or from its external application to sores.

Lastly, long-continued irritation of the skin and the accompanying hyperæmia may result in a general discoloration which has been confused with that of Addison's disease. Greenhow laid stress on that seen in "elderly persons of very indigent circumstances and uncleanly habits, especially when infested with vermin," or "vagabond's disease." In these cases the pigmentation could be partially, or wholly, removed by soap and water, and the constitutional symptoms of debility, sinking at the epigastrium, and languor, by food and tonics.

The medicinal use of arsenic, if persisted in, may lead to a cutaneous pigmentation which may have much the same distribution as that of Addison's disease.

In syphilis, also, the skin may become discoloured, and some cases of Addison's disease that have improved under a course of iodide of potash may have been of this nature (11).

The distribution of tinea versicolor should prevent any confusion between it and melasma Addisonii. In pellagra the skin may be darkened, while the dyspepsia, pains, and early paralytic symptoms might simulate those of Addison's disease; pellagra, however, is an endemic disease not met with in England (*vide* article "Pellagra," vol. ii.)

Lastly, the darkening of skin due to hereditary influences, exposure to the sun, or to tar, or to the heat of furnaces in gas-works, etc., must not be regarded as evidence of suprarenal disease. Addison's disease in blacks would be a matter of very great difficulty. Dr. W. S. Thayer has kindly given me the details of a negro who died with tuberculosis, the primary focus being on one of the adrenals, in the Johns Hopkins Hospital. At the autopsy Professor Welch thought there was a definite relation between the primary lesions and the rather excessive pigmentation of the gums, palate, and tongue. Beavan Rake (41) described Addison's disease in a syphilitic Hindoo, who was also the subject of leprosy.

Addison's disease without pigmentation can only be diagnosed after the elimination of any other satisfactory cause. A few such conditions may be mentioned. Gastric disorders, especially some cases of carcinoma leading to vomiting and asthenia, may resemble Addison's disease without pigmentation. Osler (38) speaks of difficulty having arisen in distinguishing some cases of typhus from Addison's disease. Pernicious anæmia does not present the facies of Addison's disease, and in any case of doubt its characteristic blood changes would at once settle the question. The early stages of splenic anæmia—the extreme debility, and the loss of muscular power—perhaps resemble Addison's disease; but on examining the abdomen the splenic enlargement would be detected at once and would thus prevent any mistake. In Addison's disease the spleen is sometimes found enlarged at the autopsy, but it is rarely a clinical phenomenon, and has no resemblance to that seen in splenic anæmia.

The debility and sickness in those exceptional instances of Bright's disease, in which a low-pressure pulse is found, would be accompanied by œdema and albuminuria, and so would be distinguished at once from Addison's disease.

Treatment.—The treatment naturally falls into two categories :—

1. The special form of treatment by suprarenal gland substance in various preparations. An attempt is thus made to combat the results of suprarenal inadequacy; and,

2. The symptomatic treatment on general principles.

Suprarenal extract.—It was administered first by subcutaneous injection in the form of an extract or juice. Oliver and Schafer (45) have shown that the activity of the extract is not in any way impaired by pepsin and hydrochloric acid, so that the simpler and more convenient method of giving it by the mouth should be equally efficacious. Raw sheep's suprarenal bodies have been given, and a tincture has been prepared and given by the mouth; but the most convenient form is a dried extract in the form of pills or tabloids, 1 gr. of pill corresponding to 15 grs. of the gland substance. The glands of the sheep are usually employed.

The treatment should be begun by one pill, equivalent to 15 grains of the gland substance, three times a day. The amount should be gradually but considerably increased. Since no bad results have yet been observed it is possible that they are not prescribed in sufficient amounts. Ringer and Phear (42) gave their patient as much as 2 drachms of suprarenal substance daily with benefit. No cases have been recorded in which bad results could be definitely ascribed to the use of the extract, but such a possibility should not be forgotten. Dr. Osler (40a) has recounted a case in which a girl with Addison's disease died on the 9th day of treatment with delirium and collapse. The quantity of the glycerine extract (equivalent to half a gland per diem) given was not excessive, and since patients die with these symptoms without such treatment, it did not appear that death was due to the toxic effect of the extract. It should be remembered in this connection that the medulla alone contains the active physiological principle, the cortex appearing to be inert; and that the extract is at present largely made from the whole gland, and not, as would be physiologically more correct, from the medulla alone. This must lead to a certain amount of uncertainty as to the amount of active principle contained in any pill or tabloid.

Ringer and Phear have collected the results of the treatment of Addison's disease by suprarenal gland substance. As compared with the effects of thyroid treatment in myxœdema they are at present disappointing. The results vary; sometimes there is no perceptible improvement, but the general tenor is of temporary improvement in strength and appetite, and some diminution in pigmentation; but relapse takes place even though the treatment is continued. In some instances remarkably good results have been obtained; it should be borne in mind, however, that the course of the disease is sometimes much prolonged. It is highly desirable that the future progress of such cases should be recorded as well as the immediate result. Dr. G. Oliver (35) has mentioned, and the same thing has occurred in a case under my care, that when the treatment is interrupted the pigmentation increases. It appears that, as in myxœdema, the treatment should be continued and not remitted when improvement, however well marked it may be, takes place. Dr. Byrom Bramwell, who regards the symptoms of Addison's disease as partly due to glandular inadequacy and partly the result of irritation of the sympathetic in the neighbourhood of the suprarenal bodies, explains the failure of the extract in some cases by supposing that in these instances there are adhesions to the sympathetic plexus and irritation of it; while the cases which react satisfactorily to the extract are those in which there is only glandular inactivity or inadequacy.

General lines of treatment.—When there is marked muscular weakness and debility the patient will naturally keep in bed; but even apart from this the slightest tendency to syncope should be regarded as an urgent indication for perfect rest in the horizontal position. Death has occurred from this cause long before asthenia had become a prominent feature. Great care should in such cases be exercised in raising the head. During an exacerbation of the symptoms, and for some time after, the patient should be kept in bed. Worry, over-exertion, exposure to cold, and all danger of exhausting the patient's feeble strength, should be vigilantly guarded against.

A simple, easily digested, and nutritious diet should be provided, and constipation warded off on the one hand, and diarrhœa on the other.

Strong purgatives should be avoided, from the danger of syncope resulting from shock after their use; in one case, quoted by Dr. Greenhow, the administration of a purge rapidly led to a fatal issue in a case of Addison's disease previously latent. Diarrhœa should be restrained by opium, bismuth, or other appropriate remedies.

Vomiting may be almost incontrollable in some cases, and rapidly brings about a fatal termination. Ice, fluid food in small quantities frequently repeated, effervescing draughts, soda water, and champagne may be given to combat it. As drugs, oxalate of cerium, bismuth, nd opium should be tried. Hydrocyanic acid may act as a cardiac epressant.

Tonics such as strychnine, arsenic, or iron, if there be anæmia, may be iven; and if the stomach will tolerate it, some palatable combination of od-liver oil, maltine, should be tried. Stimulants will almost always be equired.

Oestreich has recorded a case in which surgical removal of a tuberculous suprarenal body was followed by disappearance of symptoms resembling those of Addison's disease. Before the operation a mass regarded as enlarged glands was felt close to the spine and was thought to be the cause of the symptoms. If the symptoms were due to the tuberculous adrenal they must have been the result purely of irritation of the sympathetic and not in any way due to suprarenal inadequacy.

REFERENCES

1. Abelous and Langlois. *Archives de Physiol.* 1892.—2. *Idem.* *Soc. de biolog* 1891, 1892.—3. Addison. *On the Constitutional and Local Effects of Disease of the Suprarenal Capsules.* London, 1854.—4. *Idem.* *London Medical Gazette* (new series), vol. viii. 1849, p. 517.—5. Alexander, C. *Ziegler's Beitrage*, vol. xi. No. 8.—6. Alexais and Arnaud. *Revue de médecine*, 1891, p. 281.—7. Allchin. *Trans. Path. Soc. London*, xlii. p. 302.—8. Andrewes. *St. Bart.'s Hospital Reports*, vol xxvii.—9. Boinet. *Rev. de méd.* 1897, p. 136.—9*a*. Byrom Bramwell. *Brit. Med Journal*, 1897, vol. i.—10. Brown-Sequard. *Journal de la Physiologie*, 1858.—11 Debove and Achard. *Manuel de médecine*, vol. vi. p. 937.—12. Fenwick, B *Trans. Path. Soc.* vol. xxxiii. p. 351.—13. Fitz. Pepper's *Text-Book of Medicine*, vol. ii. p. 977.—14. Foa and Pellacani. *Archiv. della scienz. med.* vol. vii. fasc ii. 1883.—15. Garrod, A. E. *Journal of Physiology*, vol. xiii. p. 598.—16. *Idem* *British Medical Journal*, 1895, vol. i. p. 747.—17. Geoffredi and Tinno. *Riforma Med.* April 15, 1895.—18. Gourfein. *Rev. méd. de la Suisse rom.* March 20, 1896. —19. Greenhow, H. *Croonian Lectures at Royal College of Physicians.* London, 1875.—20. Haddon. *Trans. Path. Soc. London*, vol. xxxvi. p. 436.—21. Halliburton. *Science Progress*, Feb. 1896.—22. Hanot and Chauffaud. *Revue de médecine*, 1882, p. 386.—23. Hansemann. *Berl. klin. Woch.* April 6, 1896.—24 Harley, G. *Brit. and For. Medico-Chirurg. Rev.* vol. xxi. p. 204, 1858.—25. Hilton Fagge. *Principles and Practice of Medicine.*—26. Kahlden, v. *Virchow's Archiv*, Bd. cxiv. S. 91.—27. Langlois. *Archives de Physiol.* 1892.—28. *Idem.* *Dict. de Physiol* 1895, vol. i.—29. Legg, Wickham. *Trans. Path. Soc. London*, vol. xxxv. p. 367. —30. MacMunn. *British Med. Journal*, 1886, vol. i.—31. *Idem.* *Phil. Trans.* 1886 —32. Mann, D. *Lancet*, 1894, vol. i. p. 652.—33. Marino-Zucco and Dutto *Bull. della r. Accad. med. di Roma*, 1891.—34. Mott. *Trans. Path. Soc. London* vol. xxxvii.—34*a*. Muhlmann. *Deutsche med. Wochenschr.* 1896, Bd. xxviii.—34*b* Oestreich. *Ztschr. f. klin. Med.* Bd. xxxi. S. 123.—35. Oliver, G. *Pulse Gauging* London, p. 89.—36. *Idem.* *British Medical Journal*, 1895, vol. ii. p. 653.—37 Oliver, T. *International Clinics*, Philadelphia, vol. ii. (4th series), p. 23.—38. Osler. Pepper's *Text-Book of Medicine*, vol. ii. p. 234.—39. *Idem.* *Text-Book of Theory and Practice of Medicine by American Teachers*, 1894, vol. ii. p. 237.—40. *Idem.* *International Med. Magazine*, vol. v. No. 1.—40*a*. *Idem.* *Johns Hopkins Hosp. Bull.* Nov.-Dec. 1896, p. 208.—41. Rake, Beavan. *Lancet*, 1889, vol. ii. p. 214.—42. Ringer and Phear. *Trans. Clin. Soc. London*, vol. xxix. p. 68.—43. Rolleston. *British Medical Journal*, 1895, vol. i.—44. Schafer. *British Medical Journal*, 1895, vol. i.—45. Schafer and Oliver. *Journal of Physiology*, vol. xviii. p. 202.—46. Semmola. *Trans. Internat. Med. Congress*, 1881, London, vol. ii. p. 71.—47. Spencer, H. *Trans. of Obstetrical Society of London*, 1892, p. 276.—48. Stilling. *Rev. de méd.* 1890, p. 830.—49. Thiroloix. *Bull. Soc. anat. de Paris*, Feb. 2, 1894.—50 Thudichum. *Report of Officer to the Privy Council*, 1868.—51. Tizzoni. *Ziegler's Beitrage*, vol. vi. No. 1, 1889.—52. Trousseau. *Clinical Lectures*, vol. v. p. 150.

New Sydenham Society.—53. Vincent, S. *Birmingham Medical Review*, August 1896.—54. Wainwright. *Trans. Path. Soc. London*, vol. xliv. p. 137.—55. West, S. *St. Bart.'s Hosp. Reports*.—56. Wilks, S. *Guy's Hospital Reports*, 1859, 1862, 1865. —57. *Idem.* Reynolds' *System of Medicine*, vol. v. p. 359.—58. White, Hale. *Journal of Physiology*, vol. x. p. 345 ; 1889.

OTHER DISEASES OF THE SUPRARENAL BODIES

In the preceding article on Addison's disease reference has been made, incidentally, to many morbid conditions of the suprarenal bodies. Although certain of these changes need not necessarily give rise to clinical symptoms, it is desirable, nevertheless, to include a general account of them in a system of medicine.

Atrophy of the suprarenal bodies.—The organs vary considerably in size, but they are relatively larger in early life. They share in the general growth of the body, and as old age approaches participate in its involution.

Occasionally atrophy takes place without any evidence of inflammation, and may be so extreme as to reduce them to the size of peas. In such cases all the symptoms of Addison's disease may be present (*vide* p. 544).

Fatty change.—In the suprarenal bodies of adults fatty change is so common as to be a physiological condition. The fat occurs as large globules in the cells. This change may be present throughout the whole of the cortex, or be best marked in the zona fasciculata. The medulla is occasionally seen to be occupied by fat, but never to the same extent as the cortex; while in children there is little fat normally. Attlee found, however, some, though slight, fatty change in still-born children. In children dying from marasmus there was marked fatty change, which was more frequent than in the liver. The cortex was affected in all, and the medulla in six out of the nine. Experimentally he found that starvation, suppuration, or poisoning, whether acute or chronic, gave rise to marked fatty changes.

Fatty change does not give rise to any symptoms.

Hæmorrhage into the suprarenal capsules.—As the result of severe injuries, such as fracture of the spine or rupture of the liver and spleen, blood is often poured out around the suprarenal bodies. Hæmorrhage into the suprarenal bodies is not infrequently met with under these conditions, and is almost always into the medulla.

As the result of traumatism during birth, hæmorrhages frequently occur into the suprarenal capsules. On an examination of 130 still-born children Dr. H. Spencer found extravasations into these organs in 26; in 2 of these the hæmorrhage had occurred in the cortex, in the remaining 24 into the medulla; in half the cases it was bilateral; in 3 cases the hæmorrhage had ruptured the capsule. These hæmorrhages occurred more often in difficult labours, and were more frequently met with in pelvic than in cephalic presentations.

Apart from traumatism, hæmorrhage into the medulla of the suprarenal capsules has been recorded in a variety of conditions, in which the most common factor is chronic venous congestion. In a few cases hæmorrhage has been associated with definite symptoms, such as pain in the back, severe collapse, or even Addison's disease.

Lardaceous disease.—When attacked by lardaceous disease the suprarenal capsules appear but slightly increased in size, and have a somewhat translucent appearance on section. With the iodine test the cortex becomes a dark brown, while the medulla remains of a gray or grayish yellow. The contrast thus presented is the reverse of that seen in health. The suprarenal bodies are among the organs which undergo the lardaceous change with comparative frequency. In twenty-one cases of well-marked lardaceous disease the suprarenal capsules were affected in nine; in four of the cases it was so slight that microscopic examination was necessary to determine its presence. According to Cornil and Ranvier it is rare, and only attacks the vessels of the medulla. In my cases, however, it was always best marked in the vessels running vertically through the cortex; and, though it may be present in the medulla, it is always less marked there than in the cortex. Orth describes the lardaceous change as occurring chiefly in the region of the zona fasciculata.

Cloudy swelling.—Softening and cloudy swelling of the suprarenal capsules occur in febrile conditions; and it is noteworthy that the spleen and the adrenal bodies show very similar changes under these circumstances The medulla appears sodden and blood-stained, and, microscopically, small extravasations may be found in the cortex. The softening disposes to a separation between the cortex and the medulla, and thus even slight manipulation may produce a cavity. This finds a permanent record in the name "capsule" as applied to the suprarenal gland.

In pyæmia small vascular streaks in the cortex, or more rarely minute abscesses due to embolism, may occur.

Tubercle.—In generalised tuberculosis miliary tubercles may be seen in the suprarenal bodies.

In chronic tuberculosis, whether primary or secondary, the process begins on the medulla. Care must be taken not to regard as discrete caseous tubercles the small fatty adenomata so often seen projecting from the cortex.

In the early stages of chronic tuberculosis the inflammatory granulation tissue has a firm speckled appearance, and, microscopically, contains numerous vessels. Caseation, softening, or calcareous infiltration may all follow as in other tuberculous formations; but it is highly improbable that caseous material is ever absorbed or disappears. Tubercle is frequently found without any signs or symptoms having been present.

In 157 cases of tuberculous disease of various parts of the body, secondary tuberculous caseous foci were found in 20 without any signs of Addison's disease. Arranging the cases in decennial periods, it is seen that in 25 cases in which death occurred under 10 years of age no tubercle was found in the suprarenal bodies; in 18 cases occurring between the ages of 10 and 20 years tubercle was found five times; in 34 cases between 20 and 30 years three times; in 36 cases between 30 and 40 years seven times; in 25 cases between 40 and 50 years once; in 12 cases between 50 and 60 years twice; in 6 cases between 60 and 70 years twice. There appears, therefore, to be a marked immunity from tubercle during the early years of life, that is, at a time when the suprarenal bodies are relatively larger, freer from fatty change, and possibly more active than in later life.

Syphilis.—Single or, more rarely, multiple small gummata are occasionally seen in the suprarenal bodies, and general fibrosis may be due to the syphilitic poison.

Simple tumours of the suprarenal bodies may be divided into two groups: (*a*) adenomata which are not uncommon, and (*b*) cysts and other rare growths.

Adenomata.—Several kinds of adenomata occur; the first two, especially the first, are common, the others are rare.

i. Multiple small yellowish nodular projections, situated on the cortex of the organ; they are not marked off by any capsule from the surrounding tissue, but differ from it in being the seat of very advanced fatty change. In other respects the cells composing them are like the cells of the cortex. These adenomata pass by gradual transitions into the irregularities often seen in the suprarenal bodies of adults. They are sometimes mistaken for tubercles undergoing caseation; in this connection it is well to remember that chronic tuberculosis begins in the medulla.

ii. Large adenomata are almost always found singly in the suprarenal capsule, though they may be bilateral. Virchow described them under the name of "struma lipomatosa suprarenalis"; and recently from analogy they have been named adrenal goitres; though it must be regretted that a name of such purely local application as goitre should be applied to a tumour in the abdomen. They do not involve the whole of the organ, but form distinctly localised tumours which may attain a very considerable size. They arise in the cortex, and in arrangement usually resemble the zona fasciculata. They are a magnified edition of the small multiple suprarenal adenomata. Small ones may coexist with them in same organ. The cells contain a large amount of fat, and this accounts for the pale yellow colour of the adenomata. Occasionally the fatty change is so advanced that they appear softened or necrosed. When this is the case, some extravasation may occur into the substance of the organ. Commonly they have no more supporting fibrous tissue than the rest of the organ; but in other cases the quantity of fibrous tissue is much in excess, so that the term fibro-adenoma may be used. I have seen an example of this variety in which the cells did not show any fatty change, and in which hyaline degeneration of the vessels, which were numerous, was well marked.

iii. Diffuse fatty adenomata arising from the cortex and containing much blood are described by Letulle. To the naked eye they resemble malignant growths, but differ from them in not infiltrating the tissues, or leading to secondary growths. They are probably an exaggeration of the preceding kind. According to this author, they have been erroneously described as angio-lipomata and sarcomata.

iv. Pigmentary adenomata arising from the zona reticularis. The cells contain pigment granules, but never show fatty change. They may be multiple. Letulle described three cases, all in phthisical subjects.

v. Adenomatous tumours of the medulla containing numerous vessels and epithelial cells. The veins may contain the hyaline material found in the veins of the medulla by Manasse (7). These tumours are rare, and, as they have probably been described sometimes as sarcomata or gliomata, some doubt exists as to their classification.

Cysts.—Cysts in the suprarenal body are very rare; the occurrence of echinococcus may be mentioned, and cysts the result of former hæmorrhages have been met with. I have seen a cyst the size of a cherry containing tenacious fluid. Virchow has suggested that cysts may be formed by a softening down of adenomata of the suprarenal capsules.

Other tumours of the suprarenal bodies, such as fibromata, fibromyomata, ganglionated neuroma, and angioma, have been recorded, but are pathological curiosities.

Simple tumours arising in accessory suprarenal bodies, or in suprarenal "rests."—Accessory suprarenal bodies are very commonly present in the connective tissue in the immediate neighbourhood of the two organs. They are found when looked for; but otherwise, as they are so small, they do not, as a rule, attract attention. They are yellow in colour, oval or round, and usually about the size of a grain of corn. I have seen one as large as a cherry, but this is very exceptional.

The accessory suprarenal bodies may be found among the fibres of the renal or solar plexus and in close relation to the semilunar ganglia.

They have been found in the broad ligament of the uterus, on the spermatic vessels near the inguinal canal, and even the epididymis. The larger accessory suprarenal bodies contain a medullary portion, and Eurich has described a tumour arising in the medulla of an accessory suprarenal body.

Instead of being in the loose connective tissue, accessory suprarenal bodies may be found embedded in the kidney or liver, and are then often spoken of as suprarenal "rests." Though Schmorl records four examples of suprarenal "rests" occurring in the liver in 510 examinations, they are much more commonly recognised in the kidney than in the liver. Personally I have failed to find them.

In the kidney, by taking on adenomatous growth, they may give rise to innocent tumours; some so-called renal adenomata and "lipomata" are thus explained (4). In the case of "lipomata" the adenoma of the suprarenal "rest" undergoes extensive fatty change. Reference will be made later to malignant tumours arising in suprarenal "rests."

Malignant disease.—*Primary.*—Both sarcoma and carcinoma are described, and tumours conforming in structure to a glioma have been recorded as arising from the medulla. The tumours are usually hæmorrhagic and soft, have a tendency to undergo fatty degeneration, and frequently contain necrotic areas and hæmorrhagic cysts. Letulle, as already mentioned, has described, under the name of diffuse adenoma, growths of a somewhat similar structure, but without any tendency to infiltrate the surrounding parts. It must be admitted that there may be considerable difficulty in determining whether a tumour of the suprarenal body, undoubtedly malignant as shown by the presence of secondary growths, should be referred to the sarcomata or to the carcinomata.

Malignant disease of the suprarenal body may spread into the suprarenal vein, and so into the renal vein or inferior vena cava. The growth may eat its way directly into the upper part of the kidney, and, by involving the pelvis, may give rise to hæmaturia, and so simulate a primary lesion of the kidney. On the right side it may directly invade the right lobe of the liver. In several cases it has displaced the colon downwards instead of carrying the gut in front of it, as is the case in renal tumours. Clinically, too, suprarenal tumours rather resemble cysts, while malignant renal tumours are usually solid. Secondary growths occur in the liver, lungs, kidneys, bones, lymphatic glands, and skin. In 36 cases collected by R. Williams, more than a third occurred in children; they may be congenital, and have been found to be bilateral. On the other hand, in 20 cases of primary sarcoma collected by Affleck and Leith the average age was 45 years. In young children precocious development of hair and of the genital organs has been occasionally noticed in connection with suprarenal growths. The temperature may be depressed, or may, on the other hand, be continually raised. Diagnosis is difficult in these tumours, and they most resemble the more commonly occurring primary growths of the kidney; in fact, when a suprarenal growth has extensively invaded the kidney, it may be difficult, even at the autopsy, to say where it began. These soft hæmorrhagic tumours of the suprarenal body may simulate hydatid cyst, a hæmorrhagic abdominal cyst, and on the left side a pancreatic cyst or disease of the spleen.

Treatment is that of malignant disease of the kidney, which it clinically resembles. H. Morris has published the details of a case operated upon by him.

Malignant tumours of other organs arising in suprarenal "rests."—Besides giving rise to "lipomata" or adenomata of the kidney, displaced accessory suprarenals or "rests" may be the origin of malignant growths in the kidney. Their structure resembles that of primary malignant disease of the suprarenal bodies, and they show the same tendency to the formation of hæmorrhagic cysts, and to undergo necrosis. Lubarsch and M'Weeney have recently given admirable summaries of our knowledge of the subject. The same difficulty arises here, as in the case of malignant disease of the suprarenal bodies, in definitely assigning the tumour either to the group of the sarcomatous or to that of carcinomatous growths.

M'Weeney, while inclining to the view that they are carcinomatous, cautiously prefers to call them "kidney tumours derived from suprarenal *rests.*"

Lubarsch has found glycogen in these tumours.

Clinically their course is usually slow at first, but they may suddenly become extremely active and rapidly cause death.

Secondary growths occur in two-thirds of the cases, most frequently in the lungs.

The only treatment is, of course, removal; but so far this has not been very successful.

Schmorl suggests that some of the primary tumours of the liver may similarly be due to active proliferation, and new growth in a suprarenal "rest" embedded in that organ. Such a view certainly explains the origin of large-celled vascular growths on the liver, and might also be extended so as to include similar retroperitoneal sarcomata.

Secondary growths in the suprarenal bodies are not uncommon. In 100 cases of carcinoma of various parts of the body secondary growths in the suprarenal bodies occurred ten times, and in 35 cases of sarcoma five times. Dr. Norman Moore, in 102 cases of carcinoma, found secondary growths in three; and in 21 cases of sarcoma five times—three sarcoma, two endothelioma. It appears probable, therefore, that secondary growths are commoner in sarcoma; this is easily explained by the extensive blood-supply of the suprarenal bodies taken in conjunction with the spread of sarcoma by the blood-vessels. The relation of Addison's disease to secondary growths in the suprarenal bodies is dealt with on page 545.

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REFERENCES

1. AFFLECK and LEITH. *Edinburgh Hospital Reports*, vol. iv. p. 278. — 2 ATTLEE. *Med. Chron.* New Series, vol. iii. p. 374. — 3. EURICH. *Journ. of Path.* vol. iii. p. 502.—4. GRAWITZ. *Virchow's Archiv*, Bd. xciii.—5. LETULLE. *Archives de Science médicale*, 1896, p. 80.—6. LUBARSCH. *Virchow's Archiv*, Bd cxxxv. p. 141.—7. M'WEENEY. *B. M. J.* 1896, vol. i. p. 323.—8. MANASSE. *Virchow's Archiv*, Bd. cxxxv. p. 263.—9. MOORE, N. *Medical Pathology*, p. 355.—10 MORRIS. *B. M. J.* 1893, vol. i. p. 2.—11. SCHMORL. *Ziegler's Beitr.* vol. vi. p. 52
—12. SPENCER, H. *Obstet. Trans.* 1892. — 13. TARGETT. *Path. Soc. Trans.* vol xlvii. p. 122.—14. WILLIAMS, R. *Lancet*, 1897, vol. p. 1261.

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HODGKIN'S DISEASE

SYNONYMS.—*Lymphadenoma*, *Lymphadenosis*, *Pseudo-leucæmia* (Cohnheim, Wunderlich), *Anæmia lymphatica* (Wilks), *Anæmia splenica* (Griesinger), *Lymphatic cachexia*, *Lymphosarcoma*, *Lymphoma*, *Lymphosarcomatosis*. French—*Adénie* (Trousseau), *Lymphadénie* (Ranvier), *Cachexie sans leucémie* (Bonfils). German—*Pseudoleukamie.*

Short description.—Hodgkin's disease is characterised by a general enlargement of one or more groups of lymphatic glands, frequently accompanied by enlargement of the spleen and anæmia. The enlargement of the lymphatic glands is due to an overgrowth of adenoid tissue, which in some cases becomes largely converted into fibrous tissue. Lymphomata, or disseminated growths of adenoid tissue, may arise in various organs, but more especially in the spleen, liver, kidneys, and alimentary canal. In the blood the red corpuscles may be diminished in number and deficient in hæmoglobin, while, in some cases, there is an increase in the number of the leucocytes.

History.—The earliest description of the general enlargement of the lymphatic glands, together with the presence of nodules in the spleen, was given by Malpighi in 1669; but apparently he did not consider that the combination of these two morbid conditions constituted a definite disease. Craigie, in 1828, defined the anatomical characters of the glandular enlargements, and pointed out how they differed from those of scrofulous enlargement and from those of cancer of the glands. To Dr. Hodgkin rightly belongs the credit of having first described, in 1832, the main clinical features of the disease which now bears his name. He described the association of the enlargement of several or of many lymphatic glands with changes in the spleen as an important characteristic of the disease. Velpeau, in 1839, described the enlargement of the lymphatic glands which was not associated with scrofula. In 1856 Sir Samuel Wilks drew attention to some cases and to their similarity to those described by Hodgkin twenty-four years before. In the same year Bonfils described a case of *hypertrophie ganglionaire générale, cachexie sans leucémie*, with an account of the necropsy, and gave a clear description of the characters of the disease. In 1858 Billroth described the structure of the enlarged glands, and Wunderlich published two cases. The following year further contributions to the subject were made by Pavy and by Cossy. Virchow gave a short description of the disease in 1864. In 1865 Wilks gave a further description of his cases and of the general characters of the disease. Cornil collected the cases which had already been observed, and recorded two others with a careful account of their pathological anatomy. The same year Trousseau devoted a chapter in his *Clinique* *médicale* to a description of the characters and nature of the disease, to which he gave the name of *adénie.* In 1866 Wunderlich gave the first thorough account of the disease in German. The year following, Muller described seven additional cases from Niemeyer's clinic. In 1870 Dr. Murchison related the history and the symptoms of the disease, and gave the results of Dr. Burdon Sanderson's microscopical examination of the diseased organs. The disease was described as pseudo-leuchæmia by Mosler in 1878. The disease was discussed at the Pathological Society of London in 1878 (*Trans.* vol. xxix.), and a most comprehensive account of the disease was given by Sir William Gowers in 1879. In 1892 Dr. Dreschfeld published a clinical lecture on acute Hodgkin's disease, which contains valuable observations upon the condition of the blood. In addition to these contributions many single cases and collections of cases have been published from time to time, to which I cannot now refer.

Etiology.—Our knowledge of the etiology of Hodgkin's disease is very scanty. Of the immediate causes we know nothing definite as yet. By some physicians it is supposed to be due to a micro-organism; and the course of acute forms of the disease is highly suggestive of an acute infective process. The present state of our knowledge of this part of the subject will be considered more fully in dealing with the pathology of the disease. When we examine the circumstances under which the disease arises we find that in more than half of the recorded cases none of the remoter causes can be traced. Thus Gowers found that in 64 out of 114 cases the patients were in good health up to the beginning of the disease, and no etiological factor could be discovered to account for the onset. In some cases, however, there are certain antecedents which appear to be concerned in the event, and to these I shall now refer.

Heredity.—Evidence of direct transmission from parent to child is almost entirely wanting. Muller recorded one case in which all the children of a father who suffered from Hodgkin's disease were subject to enlargement of the lymphatic glands. The disease shows no tendency to occur in the more distant blood relations of the patient. Tuberculosis is the only disease which appears to cause any proclivity to it, and, whether as pulmonary phthisis or as tuberculous disease of the lymphatic glands, may be found in one or more members of the same family. But when we consider the great frequency of tuberculosis we cannot assume that such cases are more than coincidences.

Sex.—The male sex is much more liable to the disease than the female; it occurs three times as often in men as in women.

Locality.—The disease occurs independently of any special local conditions, and there is no evidence that any one kind of climate favours its occurrence more than another.

Personal antecedents.—Tuberculosis.—Tuberculous disease of the lymphatic glands may dispose them to a later development of lymphadenoma; for in a few cases the onset of the disease has been preceded by scrofulous enlargement of the glands with suppuration.

Syphilis.—Three cases are mentioned by Gowers in which the onset of the disease had been preceded by syphilis, but the relationship of the one to the other is doubtful.

Parturition.—The disease rarely occurs during pregnancy, but several cases have occurred shortly after childbirth, and have run a very acute course, ending fatally within a few weeks. Parturition thus has an unfavourable influence upon the progress of the disease.

The onset has sometimes been preceded by exposure to cold. In a few instances want of food, excess of alcohol, over-exertion and mental depression appear to have contributed somewhat to the initiation of the disease.

Local irritation.—Trousseau pointed out that in some cases the enlargement of the lymphatic glands was, in the first place, due to some local source of irritation in the neighbourhood of those glands which first become affected. Thus a local glandular enlargement, due to otorrhœa, chronic nasal catarrh, and a carious tooth, has been followed by the general appearance of the disease in other glands. In other cases the disease has been preceded by an increase in the size of the respective glands in inflammation of the pharynx, inflammation of the lachrymal sac, and in soft chancre.

Varieties.—Different forms of Hodgkin's disease occur which may be classified in various ways. The chief points in which cases differ from one another are the distribution of the glandular enlargements, the consistence of the enlarged glands, the condition of the spleen and other viscera, the state of the blood, and the course of the disease. Thus in some cases one group of glands only is enlarged; in others, several groups; in others, again, almost all the lymphatic glands. When the disease is general the enlargement may be uniform, or some glands may be much more increased in size than others. In some cases the glands are soft, in others hard; but no sharp distinction can be made between the two, as both hard and soft glands may occur together in the same patient, and the glands may be hard at one stage of the disease and soft at another. It has been thought that when the glands are soft the blood contains an excess of leucocytes, and the name lymphatic leuchæmia has been applied to such cases. This distinction, however, does not hold good; for in some cases with soft glands there is no leucocytosis, while on the other hand it may exist when the glands are hard. In any of the varieties I have mentioned there may or may not be enlargement of the spleen or changes in the other organs due to adenoid growths in them. The condition of the blood varies; anæmia is nearly always present; but the leucocytes may be normal or may be excessive in number. When leuchæmia occurs, the leucocytes are chiefly mononuclear, though eosinophile cells are sometimes present also in fairly large numbers. The course of the disease varies considerably, and it is convenient to speak of an acute and a chronic form of Hodgkin's disease. Dr. Dreschfeld describes three types of the acute form: one in which the superficial glands are enlarged, a second in which the intrathoracic, and the third in which the intra-abdominal glands and abdominal organs are affected.

Symptoms.—*General.*—The most important symptoms which occur in Hodgkin's disease are enlargement of the lymphatic glands, anæmia, enlargement of the spleen, rise of temperature, progressive loss of strength and emaciation. Some other less frequent symptoms will also be considered presently. Enlargement of the superficial lymphatic glands is the most frequent of the early symptoms, as in more than half of the cases it is the first change which attracts the attention of the patient. When the glands, which are deeply situated, are enlarged early, the symptoms caused by their pressure upon the surrounding organs may occur before any other sign of the disease. Thus pain in the chest and cough, pain in the abdomen, pain or œdema of the leg, according as the thoracic or abdominal glands are first affected, may be the earliest symptoms. In other cases the general constitutional symptoms, such as anæmia, loss of weight and weakness, are the first indications of loss of health; and the glandular enlargement may not become apparent until later. Rarely an irregular form of fever may precede the glandular enlargement.

Lymphatic glands.—Early enlargement.—The superficial lymphatic glands are usually enlarged before the deeper glands; thus Gowers found in fifty-two out of seventy-eight cases that enlargement of these glands was the first detected symptom of the disease. Of the superficial groups of glands the cervical are more often enlarged at the beginning of the disease than any other group. The enlargement may be limited at first to one side of the neck. In some cases many months, or even three years, as in a case recorded by Osler, may elapse before those on the opposite side become involved. Less frequently the inguinal glands, and rarely those in the axilla, are the first to become affected.

Characters of enlargement.—The lymphatic glands increase in size at first independently of each other, and remain separate. This condition may continue until they are as large as pigeons' eggs. The skin is freely movable over the superficial glands; and in the early stages of the disease the different members of a group of glands can be moved one upon another. Later the glands often become firmly adherent to each other, as the result of periadenitis, or of the extension of growth from one gland to another. In this manner large lobulated masses or tumours are formed which may attain the size of a cocoa-nut. The consistence of the enlarged glands depends chiefly upon the rate of growth. If the enlargement take place slowly, they remain firm to the touch; if the increase in size be rapid, they are soft and contain a large quantity of lymph. As a rule the enlarged glands do not cause any pain, nor are they tender when pressed. Occasionally some pain may be felt in the glands if they are undergoing rapid enlargement, and an enlarged mass of glands may cause direct or referred pain by pressing upon a nerve or nerve-trunk. The progress of the enlargement varies considerably in different cases, and also in different groups of glands in the same patient. Thus enlargement may take place more rapidly at one time than another, or one set of glands may increase considerably in size while others remain nearly stationary. In some cases the glands get larger and larger until death takes place.

In others the growth becomes arrested, and in a small number the size of the glands diminishes before death occurs. In the neck the enlargement generally begins in the glands of the posterior triangle, or in those which lie beneath the lower jaw. The suboccipital glands are often enlarged also. Frequently the submaxillary glands are enlarged on both sides. The natural contour of the neck is then much distorted by the masses of enlarged glands, which may reach a large size and greatly increase its circumference. When the enlargement of the cervical glands is considerable, serious secondary symptoms may be produced by the pressure which they exert upon important structures in the neck. The larynx may be displaced laterally, or the trachea may be so much narrowed by pressure that great dyspnœa and even death may occur. Difficulty in swallowing and death from starvation may be caused by compression of the œsophagus. Pressure on the blood-vessels may lead to anæmia of the brain if the carotid arteries be concerned, or to venous congestion if the veins are affected. The vagus nerve is sometimes compressed, and this may lead to irregularity of the pulse and cardiac failure. The glandular growth may extend into the pharynx, so that swallowing becomes difficult and hearing imperfect. Extensive enlargement of the submaxillary glands impedes the movements of the lower jaw. If the enlargement of the axillary glands be considerable, movement of the arm is difficult. Pain and swelling may be caused by pressure upon the nerves and veins in the axilla. In the groin the enlarged glands may compress the femoral vein so as to produce œdema of the leg, or even thrombosis in the vein itself. The thoracic veins may be enlarged, and all the symptoms of an intrathoracic tumour may be present; the most frequent being spasmodic cough and dyspnœa. The organs in the chest may be compressed by the glands. The superior vena cava may be narrowed or even occluded, leading to œdema of the head and arms, when a collateral circulation may be established by the mammary and epigastric veins, as in a case recorded by Osler. When the glands in the abdomen are much enlarged they can be felt through the abdominal wall. They may press upon the inferior vena cava, or the common iliac veins, and may thus cause œdema of the legs. The solar plexus may be implicated, with bronzing of the skin, as in Sir W. Jenner's case, in which Sir W. Gowers found that the solar plexus was concerned, though the suprarenal capsules were unaffected. Dr. Coupland mentions another similar case observed by Sir J. Paget. Féréol and Osler also have each observed a case of this kind. Vomiting may be excited by pressure upon the stomach, or sciatic pain by pressure upon the sacral plexus. The enlarged glands may compress the ureters, or they may become adherent to the uterus and simulate a uterine myoma.

The Spleen.—The spleen is frequently enlarged, but the enlargement is not an early symptom, and as a rule it cannot be detected until the glandular enlargement has become well marked. The spleen never reaches the enormous size which is so frequently seen in cases of splenic leuchæmia, though it is generally large enough for the lower end of it to be felt beneath the costal margin. It sometimes extends as far as the middle line, but it rarely causes any pain or discomfort. Occasionally it is irregular in outline owing to the large size of the nodules of adenoid growth.

Circulatory system.—*Blood.*—Anæmia, which may be profound, is a common symptom. It frequently appears very early; but in some cases it may not appear until after the glands have become enlarged. The consequences of the anæmia are weariness, lack of energy, œdema of the feet or even of the subcutaneous tissues generally. Hæmorrhages may occur from the mucous membranes, and specially from the nose, in the subcutaneous tissue, or in the retina. When the blood is drawn it looks pale, but clear, if there be no excess of leucocytes. If there be an excess of leucocytes it looks rather milky. Coagulation takes place slowly and imperfectly.

Red blood corpuscles.—The microscopic appearances of the blood vary in different cases, and the anæmia is much more marked in some cases than it is in others. In many there are 50 or 60 per cent of the normal number of red blood corpuscles, while in a few severe cases they are as few as 25 per cent. Changes in the red corpuscles themselves sometimes occur both in the acute and in the chronic form of Hodgkin's disease. Small red corpuscles or microcytes may occur in varying numbers; in some cases they are numerous. Their presence may be readily determined by comparing their size with that of the red corpuscles in normal blood which have a diameter of about $\frac{1}{3300}$ of an inch. Irregular forms of red corpuscles which are generally included under the name of poikilocytes may also be observed. Nucleated red corpuscles are rarely seen. Dr. Dreschfeld found none in the cases which he examined.

Leucocytes.—In the majority of cases there is no excess of leucocytes in the blood. Thus Gowers found that out of sixty-four cases there was no leucocytosis in thirty-nine, although in twenty-five there was some excess of white corpuscles.

In normal blood five different varieties of leucocytes have been described by Ehrlich. (*a*) Lymphocytes—small leucocytes with a diameter of 7 μ, being thus about the same size as a normal red corpuscle. This form has a large single nucleus which stains deeply and is surrounded by a narrow margin of protoplasm without granules. (*b*) Large mononuclear cells several times as large as the lymphocyte. The nucleus is oval in shape, and does not stain deeply, while the protoplasm is non-granular and relatively more abundant. (*c*) Intermediate forms resembling the last variety, but having an irregularly-shaped nucleus. (*d*) These are generally described as multinuclear cells. It is only under the action of certain reagents, however, that the nucleus breaks up into parts, and normally it is a long, irregular body which, as Muir points out, is more aptly described as being "multipartite." The protoplasm contains granules which are stained by both acid and basic stains, and so these leucocytes are often called "neutrophiles." (*e*) Eosinophiles — cells about the same size as the last-mentioned variety, with a single nucleus. The protoplasm contains large refractile granules which take up acid colouring agents and stain deeply with eosin, to which property they owe their name. In healthy blood the average number of leucocytes is 6000 in each cubic millimetre. The different varieties occur in the following proportions: lymphocytes, 15 to 30 per cent; multinuclear, 65 to 80 per cent; mononuclear and intermediate forms, about 6 per cent; and eosinophiles, 2 to 4 per cent.

If there be leucocytosis, it is due to the presence of an increased number of the lymphocytes in the blood. Ehrlich considers that the presence of an increased number of eosinophile leucocytes in the blood is an important characteristic of the blood in Hodgkin's disease and in leuchæmia. Dreschfeld has found the eosinophiles to be fairly numerous in some cases, but scanty in others; and concludes, in opposition to Ehrlich, that they are not of much value as an aid to diagnosis. Dr. Kanthack considers that the eosinophile cells are of no diagnostic value either in Hodgkin's disease or in leuchæmia, because they have been found in large numbers in gonorrhœal pus, in many specimens of pus both from men and from lower animals, in sputum, and in muco-purulent nasal secretions. As the eosinophiles are much increased in numbers in splenic leuchæmia, it is probable that in these mixed cases of Hodgkin's disease or lymphatic leuchæmia, in which both lymphatic glands and spleen are enlarged with leucocytosis, the eosinophiles will be found more numerous than in the more simple uncomplicated cases.

Heart.—The action of the heart may be weak if there be fatty degeneration from anæmia. In fever the frequency of the pulse is of course increased, and it may be irregular if the vagus nerve is compressed by enlarged glands in the neck.

Alimentary system.—Lymphoid growths may develop in different parts of the alimentary canal, and also in the organs connected with it, giving rise to various symptoms according to their situation.

In the mouth the gums may be soft, pale in colour, and swollen, and blood may be extravasated beneath the mucous membrane. The tonsils may be considerably enlarged, and there may be extensive adenoid growths in the pharynx; these may cause deafness (by occluding the Eustachian tube), difficulty in swallowing, and in rare cases they may completely obstruct the pharynx so as to prevent the passage of food. The presence of lymphoid growths in the wall of the stomach leads to dyspepsia and vomiting; when there is ulceration of the growths the symptoms resemble those of simple gastric ulcer; vomiting may also be excited by the pressure of enlarged lymphatic glands upon the stomach itself. Lymphoid growths in the intestine may cause no inconvenience, or they may be accompanied by diarrhœa and hæmorrhage. Constipation may be caused by the pressure of enlarged abdominal glands upon the bowel. As a rule there are no symptoms of hepatic disorder. Obstructive jaundice sometimes occurs from the pressure of enlarged glands upon the bile-duct. The liver is uniformly enlarged, owing, in some cases, to the excessive development of lymphoid growths in the substance of the organ.

Respiratory system.—Dyspnœa is a frequent symptom; it may arise either from narrowing of the trachea by the pressure of enlarged glands, or from the anæmia. Bronchitis is often present. The lymphoid growths may give rise to crepitations which are audible in different parts of the chest, but do not otherwise interfere with respiration. Effusion into the pleural cavity often takes place, either as part of a general anasarca or as a result of pressure upon the azygos or bronchial veins.

Nervous system.—In some cases delirium and coma have occurred. One of Mosler's patients died from œdema of the brain, which he regarded as the result of a cerebral hæmorrhage. Various symptoms may be produced by the pressure of the enlarged lymphatic glands upon the nerves. Thus pressure upon the cervical sympathetic may cause inequality in the size of the pupils. Pains in the nerves of the arms and legs may also be the result of pressure. Osler has observed one case in which there was paraplegia from pressure upon the spinal cord.

Genito-urinary system.—As a rule there are no renal symptoms even when lymphoid growths are found in the kidney after death. The urine may contain traces of albumin; but anything more than this may be taken as evidence of ulterior changes in the kidney occurring as a complication. Lymphoid growths are rarely found in the ovaries or testicles. Amenorrhœa in women is common, and is probably a result of the anæmia. In some cases pregnancy has occurred after the commencement of the disease.

Temperature.—The temperature in cases of Hodgkin's disease has been very carefully studied by Gowers, who found that fever was present as a symptom of the disease itself in two-thirds of the cases in which the temperature had been taken. It is rather more frequent in acute than in chronic cases, and it occurs in nearly all patients under twenty years of age. When general swelling of the glands occurs at the beginning of the disease, fever is often an early symptom. Gowers describes three modes of pyrexia which may occur. In the first the temperature is continuously raised from two to five degrees above the normal, and only varies a degree or a degree and a half during the twenty-four hours. In the second mode there are periods, several days in duration, of high fever alternating with periods of normal temperature. In a third there are marked daily variations, the temperature rising to 101° or 103° each evening, and falling to 100° or even to normal in the morning.

Skin.—Owing to the anæmia the skin and mucous membranes are pale, often from the beginning of the symptoms. Sometimes there is a general subcutaneous œdema. Bronzing of the skin, as in Addison's disease, has been observed in a few cases, to which reference has already been made. Profuse perspiration occurs during the night in some cases.

Pathological anatomy.—The most important morbid changes in cases of Hodgkin's disease are enlargement of lymphatic glands, enlargement of the spleen, and the presence of nodules of adenoid growth in various organs of the body.

Lymphatic glands.—The most striking feature of the morbid anatomy of Hodgkin's disease is the enlargement of the lymphatic glands. In health the lymphatic glands may be conveniently divided into primary, secondary, and tertiary groups. Of these the primary and secondary are always to be found, whereas the tertiary glands are usually so small that they may escape observation; but they become enlarged under special circumstances. The inguinal glands are a primary group, the popliteal are secondary glands. Gulland states that in the axilla there are tertiary glands which ordinarily only measure 1 or 2 millimetres in diameter, but which in woman during lactation become temporarily enlarged. They afterwards disappear, as Stiles has found, by a process of fatty involution. These tertiary glands may also become enlarged if carcinoma develop in the mamma. It would appear from Baylis' experiments that under special circumstances entirely new glands may be formed to take the place of others which have been removed.

In Hodgkin's disease the extent of the lymphatic enlargement varies considerably in different cases. In some it is confined to a few groups of glands; in others a large number are involved. The primary lymphatic glands are the most liable to be enlarged. The cervical glands are more frequently affected than any others; after these in order of frequency come the axillary, inguinal, retroperitoneal, bronchial, mediastinal, and mesenteric glands. In addition to these, smaller groups of the secondary glands are often affected along with the primary groups with which they are connected. Thus with the inguinal the popliteal glands, and with the axillary the epitrochlear glands may be affected. Tertiary glands may also become affected, and thus large glands may be found along the line of lymphatic vessels in unusual situations; as, for instance, beneath the pectoral muscle. The same set of glands is usually affected on both sides of the body, but the enlargement may be greater on one side than on the other, or may affect one side only. A single gland may become as large as a hen's egg, and a group may reach the size of a cocoa-nut. The enlarged glands are oval in shape, and movable in the earlier stages of the disease.

Later, adjacent glands become firmly adherent either by the direct extension of the adenoid growth from one gland to another, or by adhesive inflammation of the capsules of the glands and the surrounding tissues.

The enlarged glands may be either soft in consistence or firm. The consistence does not depend upon their size, as both large and small glands may be either soft or hard. On section the colour is a grayish-white, with red spots at the points where dilated vessels have been severed by the knife, or where hæmorrhages have taken place. In some cases where the glands are firm a considerable quantity of fibrous tissue can be seen on section. Sometimes a gland is found to be caseous, but this is exceptional. When the cut surface of a soft gland is scraped, a juice is obtained which contains lymphocytes, larger cells which are often multinuclear, red corpuscles, and spindle-shaped cells from the walls of the vessels. The firm fibrous glands, when scraped, yield little or no juice.

In the neck the glands which lie above the clavicle are most frequently affected, and may reach a large size. The glands along the sterno-mastoid muscle, the submaxillary and the suboccipital glands may be affected. Chains of enlarged glands may also connect this group with the axillary or with the intrathoracic group of glands. Various secondary effects may be produced by enlargement of the cervical glands; the larynx may be pushed to one side, the trachea may be narrowed, the internal jugular vein may be compressed and thrombosed, or the recurrent laryngeal nerve may be involved. The glands in the axilla are frequently affected, and may reach a large size. They are generally enlarged on both sides of the body, but to a greater extent on one side than the other.

In the thorax the anterior mediastinal glands are often found enlarged, and may form a mass extending the whole length of the pericardium. In some cases the growth extends into the region of the thymus or into the pericardium. Both the heart and the left lung may be pushed out of place by the enlarged glands. The bronchial glands often form large masses which may compress the bronchi to a considerable extent, and the growth may extend into the lung itself. When the glands of the posterior mediastinum are affected they rarely cause any compression of the aorta, œsophagus, or thoracic duct; though in some cases the wall of the œsophagus or even the vertebræ may be involved by the growth of the glands. In the abdomen the glands most frequently affected are those which lie behind the peritoneum along the spine. The pelvic glands may also be enlarged and compress one of the ureters. Gowers mentions one case, recorded by Bonfils, in which the lumbar and pelvic glands together weighed eight pounds. The mesenteric glands are seldom affected, and when diseased they do not reach any great size. The inguinal glands are enlarged in about 50 per cent of the cases, and often form large masses in the groin, compressing both vessels and nerves in that region.

Microscopical appearance of enlarged glands.—In the early stages of the glandular enlargement, when the glands have not increased much in size and are soft in consistence, the various parts, as seen in the normal gland, are easily made out. The cortex, medulla, follicles, and septa maintain their normal relationships; but the lymphocytes, which lie in the meshes of the reticulum of the gland, are greatly increased in numbers. In some specimens, which are probably examples of a more advanced stage of the process, the cells are seen to have penetrated the septa and caused their division. A section of such a gland shows a uniform structure consisting of a fine network of fibrils, the spaces of which are filled with leucocytes, which can be washed out, leaving the stroma with a few nuclei behind. The network, which Schultz thinks is formed by the splitting-up of the septa by the multiplication of the cells which penetrate them, is irregular in form, and the spaces may contain single lymphoid cells, or groups of six or more cells closely packed together. The cells present the same appearance as ordinary lymphocytes. Sometimes multinuclear cells are seen as a result of nuclear multiplication without cell division.

In the firmer glands there is an increase in the fibrous tissue stroma as well as multiplication of the cells. The septa which run between the follicles are thickened, as are also the fibres of the medullary network.

In some the process of fibrosis continues till the gland becomes hard and firm in consistence. The cells are then present in much smaller numbers, there is a large excess of fibrous tissue in the stroma, and the capsule is thickened. Finally only a mass of fibrous tissue may remain in the place of the adenoid tissue of the gland (G. Sharp).

Spleen.—In a large majority of the cases the spleen is diseased. In 100 cases in which the condition of the spleen was noted, it was found affected in 78. In the other 22 no change was described. This organ is thus more or less changed in four-fifths of the cases. The enlargement, as a rule, is only slight or moderate in degree; in a few rare cases it has reached a large size. The weight, however, is seldom more than thirty ounces. The enlargement may be a simple hypertrophy, or it may be due to the presence of lymphomata of various sizes in the substance of the spleen. In 78 cases in which the spleen was affected, these growths were found in 57; in the remaining 21 it was only described as being enlarged. When there is simple increase in size of the spleen it is generally firm in consistence; it may be hard, but it is rarely soft. The Malpighian corpuscles are often easily seen, being rather larger than in a normal spleen. When the lymphoid growths which originate in the Malpighian bodies are present, they do not, as a rule, cause any great enlargement of the spleen. They vary in size and may be no larger than peas, or as big as crab-apples. The appearance of the growths is peculiar, and they have been compared to masses of suet or cold fat. In one case, in which I made the post-mortem examination, the cut surface of the spleen which contained these growths resembled a piece of brawn in appearance. The masses are often irregular in shape, and may even bulge out the capsule of the overlying spleen. Infarctions also are often seen in the spleen: their appearance varies with their age; if seen early, they are red, and are surrounded by an area of congested splenic tissue. Later they become pale red, and ultimately cream-coloured. Chronic inflammation of the capsule of the spleen is not uncommon, and leads to the formation of adhesions to surrounding organs and thickening of the capsule itself.

When the spleen is examined microscopically the fibrous trabeculæ are found increased in size owing to an increase in the amount of their fibrous element. The lymphoid growths which are developed in the Malpighian corpuscles resemble the enlarged lymphatic glands in structure. As in them there is a reticulum, in the meshes of which lie small round cells. New fibrous tissue is developed in which the connective-tissue corpuscles are seen; the amount of fibrous tissue may increase till the Malpighian bodies consist almost entirely of it. In this stage the lymphoid cells are few in number. Round the edges of the Malpighian bodies may be seen masses of brown pigment: this pigment is derived from degenerated and broken-up red blood corpuscles which were included in the growth of the fibrous tissue. When the nodules of new growth are large, they compress the surrounding splenic pulp; it is then frequently atrophied, and contains cells which have undergone fatty degeneration and granules of pigment. In some cases there is hyperplasia of the splenic pulp. Lardaceous degeneration of the spleen has rarely been observed.

The medulla of bones is sometimes altered, but in other cases it is normal. Changes in the medulla may or may not be associated with leuchæmia during life. By microscopical examination it has been determined that the altered condition of the marrow is due to a growth of adenoid tissue in the place of the normal bone marrow.

Alimentary canal.—Along the whole length of the normal alimentary canal are scattered numerous patches of adenoid tissue. In almost any of these centres a development of lymphadenoid tissue may take place in Hodgkin's disease; and, once started, it may extend considerably beyond the original patch. The follicles at the back of the tongue may be enlarged, and the adenoid tissue of which the tonsils principally consist may become considerably increased in amount, leading to enlargement of the tonsils, sometimes followed by ulceration.

Adenoid growths have been found in the mucous membrane of the pharynx and of the œsophagus. In the stomach there may be extensive overgrowth of the adenoid tissue and general thickening of the mucous membrane in consequence. Ulceration of this thickened mucous membrane may occur at several different points. In the intestines the special aggregations of adenoid tissue, which occur in the solitary glands and in the Peyer's patches, may become considerably enlarged from overgrowth of adenoid tissue. This change is most marked in the lower part of the ileum, but it may extend beyond the ileo-cæcal valve into the ascending colon. The adenoid growth may extend considerably in the mucous coat of the intestine without involving the muscular coat. The intestinal wall may be much thickened, but the lumen of the bowel is not diminished.

Liver.—In a considerable number of cases changes are found in the liver which may or may not be sufficient to cause an actual increase in the size of the organ. Most frequently lymphoid growths are found scattered throughout the liver; these are generally small, varying in size from a pin's head to a cherry-stone, and pink or gray in colour; in some cases the growths may reach the size of a cherry, but these are fewer in number. In appearance they resemble the nodules which have been already described in the spleen. On microscopical examination the minute adenoid growths are found, as elsewhere, to consist of lymphatic tissue. They lie in the interlobular spaces, but may also extend into the lobules; when a growth extends into the hepatic lobules it develops between the liver-cells, and causes atrophy of the latter by pressure.

Prof. Burdon Sanderson considers that the growth may sometimes originate in the tissue of the acinus itself. In some cases there is a general diffuse growth of nucleated tissue in the interlobular spaces, from which extensions may also take place into the tissue of the acini. Occasionally the enlargement of the liver is partly due to congestion of the capillaries. Effusion into the peritoneal cavity is not uncommon as a result of portal obstruction by lymphoid growths; in some cases the peritoneum is studded with small growths.

Respiratory system.—In the lungs, growths of adenoid tissue are found which may occur either as the result of direct extension of growth from bronchial glands already affected into the lung itself, or as separate centres of growth scattered throughout both lungs. The scattered growths which generally originate in the peribronchial lymphatic tissue are small in size, and resemble tubercles in appearance. They have the same structure as the growths in other organs, and seldom soften or break down. Effusions into the pleural cavity are found in some cases, and may contain blood. Adenoid growths are rarely found beneath the pleura.

Heart.—The heart is often small, and fatty degeneration of the muscular wall is not uncommon. Occasionally adenoid growths have been found in the substance of the heart or on its surface.

Genito-urinary system.—Lymphomata, similar in structure to those which are found in other abdominal viscera, occur also in the kidney. These are usually small in size, and rarely grow larger than a cherry. The growths generally develop between the tubules in the cortex of the kidney, and as they enlarge they may, by pressure, cause atrophy of the epithelium lining the tubules. The kidney may be enlarged as a whole; it is, as a rule, pale in colour, and sometimes it is the seat of fatty or lardaceous degeneration. The testicles, like other glands, may contain lymphoid growths, which lead to atrophy of the epithelium by compression. The ovaries are rarely affected.

Ductless secretory glands.—The thymus may be enlarged, or it may contain adenoid growths, which may extend to the surrounding parts. More frequently the anterior mediastinal glands are primarily affected, and the thymus by extension of the growths from them.

The suprarenal capsules were affected in one case recorded by Gowers. The thyroid gland may also be involved (Stengel).

Nervous system.—Lymphadenomatous growths occasionally occur in the dura mater, but rarely in the brain or any other part of the nervous system.

Skin.—In rare cases adenoid growths have been found in the skin.

Pathogeny.—We have as yet very little definite knowledge of the pathogeny of Hodgkin's disease. Experimental research, which of late, has thrown so much light upon the nature of many obscure morbid processes, has not as yet succeeded in elucidating this complex problem. The study of the morbid anatomy of the disease has given us much information as to the nature and distribution of the lymphadenoid growths which form so prominent a feature in it; but as yet we possess no explanation of the abnormal development of the lymphatic glands and adenoid tissues generally in the body. An examination of the comparative anatomy of lymphatic glands shows that true lymphatic glands are found only in the higher vertebrata. In fishes, reptiles, and amphibians there are no lymphatic glands. In birds and in mammals true lymphatic glands are found. Gulland has shown that leucocytes appear in the adenoid tissue of the thymus gland of mammalian embryos some time before the lymphatic glands are developed. In man we find that the lymphatic glands are more highly developed than in any of the lower animals.

Adenoid tissue, which is the principal seat of the morbid changes in Hodgkin's disease, is widely distributed in the tissues of man. It is a specialised form of connective tissue, the fibres of which form a fine network and receive an abundant blood-supply. The special characters of adenoid tissue are found most clearly marked in certain parts of lymphatic glands known as "germ-centres"; in these germ-centres the connective-tissue fibres form a very fine network, supporting the numerous capillaries which enter it. At the periphery of each germ-centre the fibres lie close together and form a kind of capsule containing only minute openings. Leucocytes escape from the capillaries in the germ-centres into the reticulum, in which they are for a time arrested. Here they undergo division, and the young cells thus formed gradually find their way to the edge of the germ-centre, from which they ultimately escape and pass through the lymphatic gland into the general lymph-stream. The same process appears to go on in all adenoid tissue, though less actively than in the special germ-centres. Thus an important function of adenoid tissue generally, and especially of lymphatic glands, is to enable the leucocytes to multiply according to the demands of the part in which the adenoid tissue is situated.

In speaking of lymphatic "glands" it must be remembered that we are dealing with organs which differ widely, both in structure and in function, from many other organs in the body which are also called glands. The term "gland" includes all the secretory glands whose function may be either to supply an external secretion, as in the case of the salivary glands, or to produce both an external and an internal secretion as is done by the pancreas, or to form an internal secretion only like that of the thyroid gland. We have no evidence at present that lymphatic glands form any special secretion, nor from their structure should we expect them to be capable of forming any true secretion. It is important to bear this in mind; for in dealing with diseases of secretory glands we have to take into account the effect of the disease in decreasing, increasing, or altering the secretion of the gland, and the consequent effects of these changes upon the body as a whole.

We have seen that adenoid tissue generally is the seat of multiplication of the leucocytes; and when we remember the very important part which leucocytes play in the blood and elsewhere we should expect that such widespread disease of adenoid tissue as we encounter in Hodgkin's disease would modify, more or less, the production and condition of the leucocytes. An increase in the size of the lymphatic glands does not, however, necessarily bring about an increase in the number of the leucocytes in the blood; and it is in some cases only that an increased formation of leucocytes takes place in the lymphatic glands. As we do not as yet know the immediate cause of Hodgkin's disease, we can but surmise what its probable nature may be. It would seem to be due to the presence of some agent capable of exciting the growth of the adenoid tissues, and the consequent enlargement of the lymphatic glands. When we examine the known causes of enlargement of the lymphatic glands we find them to be of more than one kind. Enlargement of lymphatic glands may be a normal physiological process; thus in the axilla Stiles has found that during lactation very minute lymphatic glands become increased in size, and at the end of lactation undergo involution; so that evidently in the requirements of the mammary gland during lactation we find a cause of lymphatic activity. Many morbid processes, such as infective inflammations of various kinds, are accompanied by enlargement of the lymphatic glands connected with the part affected. There may be actual infection of the glands themselves, as in cancer or tuberculosis, leading to their enlargement; in the latter case we find the immediate cause in the tubercle bacillus. In the case of tuberculosis the lymphatic glands often form a line of defence in which phagocytes containing tubercle bacilli are arrested; these bacilli may then be either destroyed or, if they continue to live, their advance towards more important organs is arrested for a time. When we consider the many points of analogy between Hodgkin's disease and tuberculosis, and the other infective processes, it seems very probable that Hodgkin's disease is also due to infection. The clinical features of the disease, and especially the acute course of it, the hæmorrhages, the anæmia, and the presence of fever in some cases tend to support this probability. The changes which we find in the adenoid tissues and lymphatic glands are most easily explained by assuming that they are the result of the action of some pathogenetic parasite. Evidence of direct infection in Hodgkin's disease is almost entirely wanting; but one case, which was under the care of Obratzow, is of importance in this respect. An assistant, who helped to plug the nose and also to examine the urine and fæces of a patient who was suffering from acute Hodgkin's disease, soon afterwards was attacked by the same disease, and died a month after the time of the alleged infection.

Another fact which supports the infective nature of Hodgkin's disease is the occurrence of the same disease in the lower animals: the lymphadenoma of cattle, dogs, and horses appears to be identical with that of man. In this respect again it resembles tuberculosis. In horses especially, the disease presents many of the same symptoms as in man, for in equine lymphadenoma there is enlargement of the lymphatic glands, and in some cases adenoid growths in the spleen, liver, kidneys, and lungs. Emaciation, anæmia, and leuchæmia may also occur.

If the disease be due to infection we have as yet no knowledge of the organism which is the immediate cause of it. We do not even know whether it is an animal parasite, like the plasmodium of malarial fever, or a vegetable parasite like the tubercle bacillus. As Dr. Dreschfeld points out, there is a strong analogy between the different varieties of chronic and acute Hodgkin's disease and the various forms of tuberculosis. Though Dreschfeld found small bacilli in the kidney of one case, these were not present in specimens examined from other cases; and he was unable to obtain any growth of micro-organisms from pieces of the diseased glands placed in various culture media. The experiments of Delbet tend to show that the disease is due to a certain bacillus, but they require further extension and confirmation. This observer found a bacillus in the blood of the spleen of a woman who was suffering from Hodgkin's disease (*lymphadénome généralisé*), in which the spleen was also affected. He obtained pure cultivations of this micro-organism, with which he made experimental inoculations in a dog. Large doses of a pure culture of the bacillus were employed, and the inoculations were repeated several times at various intervals. This method of experiment was adopted by Delbet, as he considered the bacillus to be one of feeble virulence, and unable to multiply in the tissues of a healthy animal unless reinforced by repeated doses of the culture. The animal emaciated rapidly, and in fifteen days it lost more than one-fifth of its weight. When the dog was killed, a month after the commencement of the inoculations, the lymphatic glands in the mesentery and in the mesocolon, the thoracic and vertebral glands, as well as those in both axillæ and in the right groin, were found enlarged. On examining the enlarged glands Delbet was able to show that they contained the same bacillus which he had inoculated as a pure culture. On the strength of this experiment he claims to have produced a generalised lymphadenoma by inoculations of this bacillus. Other observers have found micrococci, and no bacilli, in the enlarged glands. Thus it is evident that the whole matter requires far more extensive experimental investigation before any satisfactory explanation of the pathology of this disease can be given.

Ordinary course, Duration, and Termination.—The onset of the disease varies considerably in different cases. In some there is at first only a localised swelling of one group of glands, and this condition may persist even for several years without further extension. A primary local disease may be followed at a variable interval by a general enlargement of the glands, or there may be a general enlargement of most of the lymphatic glands in the beginning. Generalisation of the disease is accompanied, or soon followed, by progressive anæmia; the anæmia may appear, however, before the glands are appreciably affected. In acute cases the onset may be marked by shivering, pains in the back and limbs, cough and expectoration, and rapid loss of strength.

In acute cases the patient rapidly becomes worse. In chronic cases the disease may remain stationary for considerable periods. The duration of the disease varies from five or six weeks, in very acute cases, to several years in the chronic forms of the disease.

Sir W. Gowers (10) gives the following table, drawn up from fifty fatal cases, in which the duration of the disease had been ascertained :—

Less than 1 year in 18 cases.
Between 1 and 2 years in 15 cases.
,, 2 ,, 3 ,, 6 ,,
,, 3 ,, 4 ,, 6 ,,
,, 4 ,, 5 ,, 3 ,,
Over 5 years . . 1 case.

Sex appears to have little or no influence upon the duration of the disease. Before middle life the duration does not vary at different ages ; it is shorter, however, in the second than in the first half of life.

Recovery may take place under treatment. This is more likely to occur in chronic than in acute cases, though marked improvement or arrest may occur even in the latter.

Sooner or later, in most cases, the anæmia becomes more intense, the patient loses strength, and dies from exhaustion. In some cases the immediate cause of death has been asphyxia from the pressure of enlarged glands upon the trachea or bronchi. Death has also taken place from starvation owing to pressure upon the œsophagus. In a few cases coma and convulsions have occurred at the end. Loss of blood and diarrhœa may also take part in bringing about a fatal termination. Death may also be the result of some such complication as pneumonia, œdema of the lungs, or pleural effusion.

Diagnosis.—The enlargement of the lymphatic glands which takes place in Hodgkin's disease has to be distinguished from other kinds of enlargement. In advanced cases the number of glands involved and the general cachexia render the diagnosis easy. In the early stages of the disease, when only a few glands may be affected and the severe constitutional symptoms not fully manifested, the enlargement has to be distinguished from those of acute adenitis, tuberculous lymphadenitis, sarcoma, and carcinoma. The disease, as a whole, has also to be distinguished from splenic leuchæmia, and from those mixed cases in which the symptoms of that disease appear in combination with those of Hodgkin's disease. In very acute cases the symptoms may resemble those of the known infections, especially when the abdominal glands are principally affected ; in these cases we may have to distinguish between acute Hodgkin's disease and typhoid fever, tuberculous peritonitis, or septicæmia ; or again, the symptoms of Hodgkin's disease may suggest purpura or pernicious anæmia.

In acute inflammation of the lymphatic glands—acute adenitis—the enlargement takes place rapidly, and the glands are painful and tender. The surrounding tissues are also frequently inflamed at the same time. A few glands only are affected, and, as a rule, they are directly connected with some part in which inflammation, suppuration, or a breach of surface open to microbes is already known. In Hodgkin's disease the enlargement is painless; it is unaccompanied by inflammation, and it frequently affects a large number of glands, not necessarily in contiguity.

Tuberculous disease of the lymphatic glands is generally limited to one or more groups. It frequently begins in glands which, like the cervical glands, are connected with some surface through which the tubercle bacillus may enter. Thus, if the enlargement of the lymphatic glands be general, it is almost certainly not tuberculous. Again, in the several groups of glands we find that in tuberculous disease there is often peri-adenitis, which leads to matting of the glands; whereas, in Hodgkin's disease, as the surrounding tissues are not inflamed, the glands remain freely movable. In tuberculous disease the glands soon begin to caseate or suppurate, the skin is implicated, it gives way, and the abscess discharges through the opening; in Hodgkin's disease the glands neither caseate nor suppurate, nor is the skin inflamed about them. Lymphadenomatous glands, as a rule, reach a larger size than tuberculous glands, probably because degenerative changes generally occur early in the latter We may note also a characteristic cachexia commonly known as "scrofulous." Not infrequently, however, when the enlargement is confined to a few glands a diagnosis cannot be made until some further manifestation of the true nature of the enlargement appears.

In the early stages of Hodgkin's disease, when the enlargement of lymphatic glands is confined to a small area, there may be a difficulty in distinguishing it from sarcoma of the glands. In sarcoma, however, there is a slow extension of the growth to neighbouring glands and into the surrounding tissues, whereas, in Hodgkin's disease, further extensions will probably arise in a different part of the body. So generalised an enlargement would not be sarcoma. In sarcoma, again, the presence of secondary or primary growth elsewhere may help to clear up the diagnosis.

By some writers the name lymphosarcoma has been used as another name for Hodgkin's disease; by others this name has been given to a special form of sarcoma of the lymphatic glands. This confusion should be guarded against. Sharp, who distinguishes between lymphosarcoma and lymphadenoma, considers that each starts from a lymphoma. If, as the tumour grows, it is found to contain very large numbers of round cells, and but little fibrous tissue, he considers it to be a lymphosarcoma. It, on the other hand, the fibrous tissue is abundant, and the cells not numerous, it is a lymphadenoma. J. L. Steven also draws a sharp distinction between primary lymphosarcoma in the mediastinum and the general affection of the lymphatic glands which we call Hodgkin's disease.

Secondary carcinoma of the lymphatic glands is not likely to be confounded with that due to Hodgkin's disease, as the presence of the primary growth indicates the true character of the glandular swelling also.

In some cases, when the nature of the enlargement of the lymphatic glands is doubtful, the administration of arsenic may aid the diagnosis. Any marked diminution in the size of the glands under the influence of this drug would indicate Hodgkin's disease rather than sarcoma or carcinoma.

Leuchæmia is, strictly speaking, only a symptom and not a disease. As a symptom we have seen that it occurs in some cases of Hodgkin's disease. This name has, however, been given to some forms of disease in which an excess of white corpuscles in the blood is a prominent symptom. Thus there are several kinds of leuchæmia, and a distinction must be drawn between these and Hodgkin's disease.

Splenic or spleno-medullary leuchæmia is distinguished from Hodgkin's disease by the absence of any early enlargement of the lymphatic glands, by the great enlargement of the spleen, and by the presence in the blood of myelocytes or large white corpuscles with a single nucleus. These corpuscles may measure nearly 16 μ in diameter; they occur in large numbers in the blood. Muir has found that in this form of leuchæmia they may form more than 50 per cent of the white corpuscles present in the blood.

In some cases of splenic leuchæmia an enlargement of the lymphatic glands takes place as a late event. The enlargement is then secondary to that of the spleen and to the leuchæmia, and thus differs from the primary glandular enlargement of Hodgkin's disease.

In another disease, "spleno-lymphatic" leuchæmia, to which Gowers draws special attention, there is a simultaneous enlargement of the lymphatic glands and of the spleen accompanied by leuchæmia. In these cases we seem to have the two diseases, splenic leuchæmia and Hodgkin's disease, combined. With the exception of the concurrent increase of the spleen such cases are closely allied to those of Hodgkin's disease, in which leuchæmia is found; and which, by some writers, have been described as cases of "lymphatic" leuchæmia.

Syphilis.—Enlargement of the lymphatic glands, most directly connected with the primary seat of infection, is a constant primary symptom of syphilis. In the male the usual primary enlargement of the glands in the groin is not likely to be mistaken for Hodgkin's disease, as in all such cases a careful inspection of the genital organs would naturally be the first step in the examination of the case, and the discovery of a sore with an indurated base would at once explain the condition of the lymphatic glands. In the female and in cases of primary syphilitic infection of other parts of the body the true cause of the enlargement might be overlooked, so that it is important in any doubtful case to remember the chief characteristics of this form of enlargement. In considering the possibility of syphilis as a cause of any glandular swelling, careful inquiry and search must be made for the presence of the original indurated sore, which develops about twenty-four days after infection has taken place, and is followed by the enlargement of the nearest lymphatic gland in seven to fourteen days. One gland is usually enlarged first, the other members of the same group becoming affected soon afterwards. The glands are hard in consistence, and seldom exceed a marble in size.

The inguinal glands on each side are by far the most commonly affected groups, but the axillary and cervical glands are involved in cases of primary infection of the upper limb or face. The enlargement rarely extends beyond the nearest group of glands, and even if untreated tends in time to subside. In Hodgkin's disease the glands soon reach a larger size, and are softer in consistence, while the disease tends to spread to other groups of glands. Some enlargement of the lymphatic glands may occur in the later stages of syphilis, but its nature would be explained by the presence of some secondary or tertiary manifestations of the disease in the neighbourhood of the enlarged glands.

Lymphoma.—A simple enlargement of a single lymphatic gland or of several glands of the same group is usually regarded as a local growth only, and as such is called a simple lymphoma or lymphadenoma. As Hodgkin's disease may also start as a similar local enlargement presenting the same characters, we are unable to separate the two in the early stages. It is not till later, when no extension of the disease occurs, and constitutional symptoms remain absent, that a distinction can be made It is quite possible that the difference between the two lies in the clinical course rather than in the nature of the disease, lymphoma being a localised form of Hodgkin's disease, the further extension of which is prevented by the natural resistance of the tissues.

Prognosis.—In cases of acute Hodgkin's disease the prognosis is very unfavourable; the patient rapidly loses strength and dies of exhaustion. Pulmonary complications frequently occur in these cases, so that pneumonia, pleurisy, or phthisis may be the actual cause of death. But acute cases are not always fatal. Dr. Dreschfeld has recorded that in one acute case with cough, fever, intense anæmia, rapid enlargement of the lymphatic glands causing obstruction of the right bronchus, enlargement of the spleen, leucocytosis and rapid loss of weight, the lymphatic glands decreased, under treatment by arsenic, nearly to their normal size: the spleen fell to its usual size, the temperature became normal, the blood improved, and the patient became convalescent. If the glands be enlarged in several regions, and reach a large size, the prognosis is grave. The actual progress of the disease is not uniform. If the patient's health has been good up to the time of the beginning of the disease, its advances appear to be less rapid than in patients in whom the onset was preceded by some ill-health. Thus in cases in which the symptoms have first appeared after pregnancy, or after a loss of blood, the downward progress has generally been more rapid than in cases in which the health had previously been good. A marked decrease in the number of red corpuscles in the blood, and a distinct increase in the number of the white, severally indicate that the case is a serious one. So long as the enlarged glands remain soft there is a better prospect of recovery. Hardness of the glands indicates fibrosis. Fever, especially if it be continuous, is an indication that the disease is acute. Œdema is a grave symptom; it generally indicates that death is not far distant.

Treatment.—In the treatment of Hodgkin's disease we have two main objects in view. In the first place, we must endeavour to combat the disease by treatment of the structures which have already become affected, so as to prevent its spreading to other parts of the body; in the second place, we have to increase the resisting power of the patient as far as possible. We have seen that in some cases the disease is local at first, tending to become general at a later stage. In this respect it resembles tuberculous disease of the lymphatic glands, in which we have abundant evidence that early local treatment is frequently successful both in curing the local disease and in averting general tuberculosis. As it is probable that Hodgkin's disease is likewise due to the presence of some infective agent, the strictly localised forms of the disease in superficial glands appear to be suitable for surgical treatment The special indications for removal of the glands will be considered presently.

General hygienic treatment.—It is important that those who suffer from Hodgkin's disease should lead quiet, regular lives and avoid all bodily fatigue. The diet should be light, nourishing, and easily digested It is doubtful whether climate has much influence upon the course of the malady, but bathing in mineral waters, as at Kreuznach or Woodhall Spa, has seemed beneficial in some cases.

Local treatment.—In certain cases of Hodgkin's disease there can be no doubt that removal of the diseased glands is the right method of treatment to adopt. The clinical course of some cases appears to indicate clearly that the disease in the first instance is local, and confined to a few lymphatic glands; moreover, that the further spread of the disease takes place from the part first affected, by a process which we may provisionally call secondary infection. In such cases the early removal of the enlarged glands may arrest the disease. One of our chief difficulties is to select the most suitable cases for such treatment. If the disease be general from the first, or if it has spread to deep lymphatic glands which cannot be removed, radical surgical treatment is no longer possible. By some physicians, however, removal of as many of the diseased glands as possible has been recommended even in cases in which several distinct groups are affected; not so much with the object of eradicating the disease, as of diminishing the number of the diseased glands in the hope that medicinal treatment may thereby be better able to deal with the remnant. In such cases, however, operative treatment has proved unsatisfactory, and when several groups of glands are affected, it is very doubtful whether partial removal is advisable. Evidence is still wanting to show that medicinal treatment is rendered more efficient by removal of some only of the enlarged glands.

Operative treatment to give relief from urgent symptoms due to pressure will be considered presently.

The most suitable cases for radical operation are those in which the enlargement is confined to one group of glands, in which the spleen is not enlarged, and in which there is neither fever nor well-marked anæmia. The presence of a few enlarged glands in other situations, or a slight enlargement of the spleen, need not preclude operation if other conditions seem favourable; but the results are not likely to be so good. It is important to take the temperature night and morning for a few days before deciding upon an operation, that the absence of fever may be definitely ascertained. Gowers considers that when the number of the red corpuscles is below 60 per cent, removal of the glands should not be attempted. A marked excess of white corpuscles in the blood is also unfavourable to operation.

The success which may attend the removal of the diseased glands in suitable cases is well illustrated by three cases, mentioned by Gowers, in which the operation was performed by the late M. Verneuil. In one case a large glandular tumour, which compressed the trachea, was removed from the neck; seven years afterwards the patient remained in good health. In another case the glands in the axilla had been enlarged for two years, and had reached the size of a child's head when they were removed. Subsequently another enlarged gland was removed from the neck, and one or two glands afterwards became enlarged and suppurated The operative treatment was supplemented by the administration of arsenic, and the patient remained free from the disease up to the time of his death, from acute pneumonia, six years after the first operation. In a third case the removal of the enlarged glands stayed the progress of the disease for some years, though it finally became generalised and ended fatally.

As already mentioned, there are certain circumstances under which an operation becomes necessary in order to relieve urgent symptoms. Thus, if the trachea, or an important nerve or blood-vessel, be compressed by an enlarged gland which can be removed, this should be done; although the operation may not be likely to check the general progress of the disease.

The difficulty of the actual operation for removal of the glands varies very much. In some cases the enlarged glands are easily separated from the surrounding structures; in others the deeper parts of the glandular mass may be adherent and the removal by no means easy.

Many other means of local treatment have been advocated and carried out in practice. None of them, however, has proved so effectual as extirpation; so that, when possible, removal is the most efficient method. Various solutions have been injected into the substance of the glands. Thus, among other drugs, arsenic, iodine, potassium iodide, silver nitrate, carbolic acid, and chromic acid have been employed. Such injections are often painful, and may lead to inflammation and suppuration of the diseased glands; very little benefit has been obtained by such methods, and the inflammation excited may prove troublesome. Galvano-puncture has likewise proved to be of little service in reducing the size of the glands. Various simple methods of local treatment have also been employed, such as massage, alternate hot and cold douching, and the application of ice. Such means of treatment are less harmful, but they lead to little diminution in the size of the glands. The application of blisters to the skin, over the enlarged glands, has in some cases been followed by a reduction in size. The application of iodine to the skin over the enlarged glands is of little or no use.

Medicinal treatment.—Of all the drugs which have been used in the treatment of Hodgkin's disease, arsenic has most frequently proved to be of service. I have seen marked improvement follow the administration of arsenic, and cases have been recorded in which the glandular swellings have disappeared, and the patient has recovered under its influence. Not only may arsenic do good in chronic cases, but even in acute cases very good results may follow its use. This is well illustrated by a case recorded by Dreschfeld: in this case there were at first marked anæmia, fever, and a slight cough. After a few days the cervical and left axillary glands become enlarged, and soon afterwards signs of obstruction of the left bronchus appeared. The spleen became enlarged, the number of leucocytes in the blood increased to a marked extent, and eosinophile cells were also found. In a fortnight the patient lost 10 lbs. in weight. Under treatment by arsenic rapid improvement took place; the temperature became normal, the superficial glands "almost completely subsided," the spleen diminished in size, the condition of the blood improved, the patient gained 14 lbs. in weight in a month, and was convalescent at the time the account was written. A very similar case under Dr. Allbutt's care recovered quickly under arsenic. Arsenic may most conveniently be given in solution; the dose being increased gradually. It is a good plan to begin with five minims of liquor arsenicalis three times a day, and this dose may by degrees be increased up to fifteen or twenty minims three times a day, provided that the patient exhibits no toxic symptoms. It should be given in milk with or just after food. If symptoms of intolerance arise, the arsenic should be discontinued for a few days. In some cases the Fowler's solution has been injected directly into the enlarged glands, but the injections may cause pain, and even inflammation and suppuration; and the results have not been so good as when given by the mouth. Reclus has recorded one case in which the cervical glands on each side of the neck were affected; arsenical solution was both given by the mouth and injected into the glands, and these diminished in size until only some small nodules remained. In two other cases this treatment proved successful, but in three others the result was unfavourable. Valuable as arsenic proves in the treatment of some cases of Hodgkin's disease, there are others in which little or no benefit appears to come from its use. The mode of action of arsenic in this disease is not known. It may have a germicidal action, comparable with that of mercury in syphilis and quinine in ague, or it may be an antidote to some chemical poison.

Iodine has been frequently used both as tincture of iodine and as potassium iodide. There is, however, but little evidence to show that it has had any useful influence upon the progress of the disease. In some cases the depressing effect of potassium iodide may be distinctly harmful. Phosphorus has been used with good effects in a few cases, but it is certainly less useful than arsenic. One patient under the observation of

Professor Allbutt recovered from a grave and apparently extreme attack of the disease while taking tungstate of soda, but this drug proved useless in all cases subsequently under his care. Mercurial inunction was found beneficial in one case by Dreschfeld, but it must be used with caution so as to avoid any symptoms of mercurialism. Iron, cod-liver oil, and quinine have been used as general tonics. Organic extracts prepared from various glandular and other tissues have of late been extensively used in the treatment of disease; but in the present state of our knowledge of the pathology of Hodgkin's disease, it is difficult to conceive that any organic extract can be of special service in the treatment of this malady. We have seen that the lymphatic glands, spleen, thymus gland, and bone-marrow are all liable to be affected in certain cases of Hodgkin's disease. For this reason both spleen and lymphatic gland and thymus extract, as well as bone-marrow, are being tried, but as yet with no very decisive result. Bone-marrow has been shown by Professor Fraser to be of great service in the treatment of pernicious anæmia in which arsenic has also proved useful, and so is worthy of trial. To an adult one ounce of fresh ox bone-marrow may be given three times a day.

George R. Murray.

REFERENCES

1. Billroth. *Beitrage zur path. Histologie*, 1858, p. 168.—2. Cornil. *Archives générales de méd.* Aug. 1865.—3. Cossy. *Echo médicale*, k.v. Neuchâtel, 1858 4. Coupland. Fowler's *Dictionary of Medicine*, p. 477.—5. Craigie. *Pathological Anatomy*, 1828, "Diseases of Glands," p. 250.—6. Delbet. *La semaine médicale*, June 1895, p. 271.—7. Dreschfeld. *British Medical Journal*, April 30, 1892, p 893.—8. Ehrlich. *Farbenanalytische Untersuchungen zur Histologie und Klinik des Blutes*, pt. i.—9. Fraser. *British Medical Journal*, June 2, 1894, p. 1172.—10. Gowers. Reynolds' *System of Medicine*, vol. v. p. 306.—11. Gulland. *Journal of Pathology*, vol. i. p. 447.—12. Hodgkin. *Medico-Chirurgical Transactions*, vol. xvii. p. 69.—13. Kanthack. *British Medical Journal*, July 16, 1892, p. 120.—14. Leslie. *Lancet*, August 24, 1895, p. 492.—15. Malpighi. *De Viscerum*, Lond 1669; *De Rene*, cap. v. p. 131.—16. Mosler. Von Ziemssen's *Cyclopædia of Medicine* vol. viii. p. 470.—17. Muir. *Journal of Pathology*, vol. i. p. 123—18. Muller. *Berliner klinische Wochenschrift*, 42, 43, 44, 1867.—19. Murchison. *Pathological Transactions*, vol. xxi. 1870.—20. Osler. *Principles and Practice of Medicine*, p 701—21. Pavy. *Lancet*, August 1859, p. 213.—22. Sharp. *Journal of Anatomy and Physiology*, October 1895, p. 59.—23. Spencer, W. G. *Pathology of the Lymphadenoid Structures*, The Wilson Lectures, Roy. Coll. Surg. of England, *Lancet* March 6, 13, and 20, 1897.—24. Stengel. *Twentieth Century Practice of Medicine* vol. vii. p. 443.—25. Steven. *Mediastinal Tumours*, p. 9.—26. Stiles. *Edinburgh Medical Journal*, 1892.—27. Thayer. *Boston Medical and Surgical Journal*, February 16 and 23, 1893.—28. Trousseau. *Clinique médicale*, t. iii.—29. Velpeau *Leçons orales de clinique*, t. iii.—30. Virchow. *Krankhaften Geschwulste*, vol. ii.—31. Wilks. *Guy's Hospital Reports*, vol. ii. 1856, p. 114.—32. *Ibid.* Third Series, vol. xi. 1865, p. 56.—33. Wunderlich. *Archiv der Heilkunde*, 1866.

G. R. M.

SCROFULA

WHEN under the teaching of M. Bazin in Paris, in the year 1859, my attention was strongly drawn by him to the subject of scrofula, and its frequency, its pitifulness, and its marring of fair young lives, served to keep the subject prominent in my thoughts. It may seem strange to my younger readers to hear that the secondary or bubonic nature of this disease was not then recognised. It was supposed to take its rise in a "vice of the system," and accordingly elaborate medicinal or magical means were wholly relied upon in the treatment of it. Of these means the only two which commanded any degree of success were cod-liver oil and sea air. Thus in the sixties and the seventies it was as common to see persons marked by the scars of scrofula as it still was to see the marks of the ravages of small-pox.

It was a common warning of careful parents that this girl or that was to be shunned as a wife because she carried on her neck this signal of a constitutional vice. I may have gone to an extreme in combating this opinion, and in declaring that scrofula is but a secondary event or "bubo," dependent upon some alien source or irritation, generally peripheral and generally avoidable; and I need scarcely say that at the time of which I speak the tubercle bacillus was neither discovered nor suspected. Whether scrofula is always due to this bacillus, or always associated with it, is not yet decided; almost up to this moment the penetration of the microbe into the tonsil and its implantation thence into the cervical glands has been a matter of doubt. It seems probable that scrofula may arise by the agency of microbes other than tubercle; again that, originating independently of tubercle, on it tubercle may afterwards supervene; and, once more, that scrofula may be due to tubercle, primarily or even exclusively. No doubt these problems will soon be settled. Meanwhile, fortunately, the practical bearings of the process are sufficiently established to perfect our therapeutics. Whether primarily tuberculous or not, eccentric irritation in the teeth, the throat, the nasal passages, the ear, the skin of the face, head, or neck may set up scrofula in the clinical sense of the word; and the enlightened practice of modern physicians, dealing more promptly and more radically with these extraneous sources of poisoning, may so prevent scrofula that our improved method of treatment by surgical means may happily be less and less in demand. Such, I think, is already the case; scrofula is far less common than it used to be. Of these susceptible peripheral parts it was always my belief that the tonsils were the most important, and I taught hypothetically that these were the prevailing sources of scrofula; that scrofula, indeed, was but the further stage of tuberculosis or suppuration of the tonsil. This opinion received little support; for some time after 1882 pathologists failed to find tubercle bacilli in the tonsils, or even in the discharges from scrofulous glands. Recently, however, this negative position has become considerably modified; pathologists doubt no longer that tubercle of the tonsil, so far from being rare, is an ordinary mode of constitutional infection, and that scrofula is a common consequence of such tonsillar diseases. In a thesis for the degree of M.D. in the University of Cambridge, Dr. Walsham recently dealt with this question fully, and produced a large series of microscopical preparations in support of his statements concerning tonsillar tuberculosis. Dr. Walsham says that the tonsils, so far from being immune from tubercle, as has been alleged, are very frequently affected by this evil. Tubercle, he says, may be primary in the tonsil, with secondary infection of the lungs or other parts, the cervical glands being often affected thus secondarily. Out of thirty-one cases of tuberculosis, acute and chronic, Dr. Walsham discovered tuberculosis of the tonsils in twenty cases. In 1884 I made the same assertion, with the use of the word "particles" instead of "tubercles," and I had insisted upon the same order of things in 1881. Koch discovered the tubercle bacillus in 1882.

Dr. Batten, another of our younger graduates, in making a general survey of the course of tubercle in the glands of children, says of the cervical glands that out of 100 cases of tuberculosis in children noted at Great Ormonde Street, the cervical glands presented evidence of tuberculous infection in fourteen. This estimate, I gather, was founded upon records of naked-eye observation only or chiefly; no doubt microscopic investigation would have increased the proportion greatly. Krueckmann found tubercle in the tonsils in 60 per cent of cases of tuberculosis, and he asserts that tuberculosis of the cervical lymphatic glands almost always depends upon the invasion of the glands by way of the tonsils. I have often surmised that the sinuses of old scrofula are likewise the seat of tubercle; I can offer no more than a surmise, but Dinochowski's results are to the same effect. Strassmann's observations led him to put the percentage higher still. Ruge arrives at the conclusion that the tonsils are an important primary seat of tuberculous infection, whether the mischief follow in the cervical glands or elsewhere. Many French observers (Peter, Cornil, Laboulbène) have brought forward similar evidence, though I have not preserved accurate references to these sources, nor is it necessary now to add to this part of the evidence. For, whether primarily tuberculous, septic or pyogenetic, that micro-organisms infect the system through the tonsils, and that in this way the cervical glands are often invaded, rest upon a strong basis of proof; and thus the etiology of scrofula leads to the recognition of the importance of prophylaxis as a fundamental part of the treatment of scrofula and as a method of preventing its implantation. Sedulous attention to any faucial disorder in children, sedulous attention to the drainage of their homes, the avoidance of aural or pharyngeal catarrhs, the removal of obstacles to free respiration, such as adenoids and the like, constitute the outworks of the campaign against this plague; and it is plain that the recognition and the revision of the conditions of health which have marked our times have already reduced the incidence of scrofula to no small extent. Nevertheless scrofula is not yet abolished, and I am tempted by my own inclination, the importance of the subject, and its bearing on the work of the pathologist, to include a section on the surgical treatment of the disease. Before passing on to this section, however, I would refer to a remarkable tract by John Browne, a surgeon of Norwich, reviewed by Mr. D'Arcy Power, in his interesting series entitled "Archæologica Medica," in the *British Medical Journal* of 31st August 1895. Browne, after some remarks on treatment by diet, and so forth, in which in many respects he seems to have been in advance of his time, says of surgical means: "These tumours (scrofulous glands) do require extirpation and extraction—to be so dexterously performed as that no part be left behind. The glands are to be extracted with great care and caution, so that every part of the cystus or bags thereof are perfectly and thoroughly eradicated and extracted, the which being done, and the part clean, mundifie the ulcer, digest, incarn, and then induce a cicatrice." "It is only in this after-treatment," says Mr. Power, "that his method differs from that of Professor Clifford Allbutt and Mr. Pridgin Teale."

T. CLIFFORD ALLBUTT.

REFERENCES

1. ALLBUTT and TEALE. *Scrofulous Neck and its Surgery.* London, 1885.—2. BATTEN, F. E. *St. Bartholomew's Hospital Reports*, vol. xxvi.—3. DIEULAFOY. "Tuberculose larvée des trois amygdalis," *Bull. Acad. Med.* 3 sér t xxxiii. 1895.—4. KRUECKMANN. *Virchow's Archiv*, Bd cxxxviii. p. 534.—5. RUGE. *Virchow's Archiv*, Bd. cxliv. 1896.—6. SOKOLOWSKI and DINOCHOWSKI. *Deutsch. Arch. klin. Med.* Bd. xlix. Hft. 6.—7. STEWART, PURVIS. "Tuberculosis of Tonsil," *Brit. Med. Journ.* May 4, 1895.—8. WALSHAM, H. *Latent Tuberculosis of the Tonsils.* Thesis for degree of M.D. Camb. May 1897.

T. C. A.

THE SURGERY OF SCROFULA

There are probably few subjects in which the ground common to the physician and surgeon is so clearly marked out as in scrofulous disease of the cervical glands, and there are few departments of surgery in which of recent years such a definiteness of aim, such a development of surgical detail, and such a profitable reward for careful work have been displayed.

Until the last fifteen or twenty years the treatment of suppurating and caseating glands of the neck was as unsatisfactory as it well could be; the resources of the physician were little more than poultices and iodine paint, and the resources of the surgeon were limited to opening with a bistoury an abscess ready to break through the skin. The result to the patient was, in the words of Professor Allbutt, that "in the continuance of his local malady over and above his faulty inheritance he ran three risks: namely, first, of a tedious local disease followed by a peculiarly unwelcome disfigurement; secondly, of a deterioration of his general health so that his best years of adolescence are spoiled, and his hold upon manhood thwarted and weakened; thirdly, of an inoculation of the system with elements which favour the dissemination of a more general tuberculosis."

The first clear note of the change which was beginning to revolutionise the practice of the physician and the surgeon in this disease was struck by Professor Clifford Allbutt in a paper which he read at the International Medical Congress in London in 1881, a paper which was followed up by the publication in 1885 of a clinical lecture, by Dr. Allbutt and myself, in which our further experience was set forth.

The mode of dealing with such glands, which at that time was scarcely known in surgery, has now become general; and able papers have been written by various surgeons discussing the details of the practice and the best methods of carrying them out. It is my intention in the present article to reaffirm the principles originally laid down, with such comments on details as the experience of myself and others may suggest.

Let me introduce the question of treatment by a definite case, which will be none the less telling that it was under the surgical care of a colleague.

In January 1880 I was requested by Mr. Wheelhouse to meet him at Dr. Allbutt's chambers, that we might consult about a fluctuating swelling in the neck of one of his patients, a young lady about sixteen years of age, and perform a radical operation if possible. There was a large soft swelling below and behind the right ear; this had been emptied of pus by incision a year before. The incision soon healed, and in spite of iodine and other applications the swelling reappeared. She had now returned home after a year at Southport with the swelling as large as ever. Hence the consultation. The decision was that the pus-containing cavity should first be emptied by the aspirator, and then if it refilled, as it probably would, that it should be opened, scraped, and drained. The cavity refilled, and in February I assisted Mr. Wheelhouse in his "radical" operation. The swelling, about the size of a duck's egg, was situated over the sterno-mastoid muscle behind and below the lobe of the left ear. Mr. Wheelhouse made an incision about 1½ inch long in the posterior border of the swelling. The pus having escaped, the subcutaneous cavity was scraped out thoroughly, and no gland was found. Now we come to the cardinal point in the surgical treatment—I may say in the radical cure—of a large number of these cases of degenerating glands. Profiting by our previous experience we searched with the point of a director, and found, as was suspected, a small hole through the deep cervical fascia that would barely admit the tip of the little finger. This led to a diseased gland in its hiding-place beneath the sterno-mastoid; the opening was enlarged, and the caseous, half-decayed lymphatic gland was unearthed by Lister's scraper. After vigorous scraping, cleansing, and washing by carbolic lotion (we had not then arrived at iodoform), a drainage-tube was inserted. The tube was left in nearly two months; its removal was rapidly followed by healing, and the neck has been perfectly sound ever since. Four years afterwards the scars of the two operations were faint white lines barely an inch long, with hardly a suspicion of dimple. Having been pallid and pasty before the operation she was now healthy and had a good colour, and her friends said "she is not like the same girl at all."

Now, what do we learn from this case? We learn first of all the absolute inutility of merely incising or otherwise opening an abscess, which probably depends on a degenerate gland which may lie beneath the deep cervical fascia.

We learn, in the second place, that the visible abscess, which would often be called a strumous suppurating gland, is merely a subcutaneous storage reservoir of pus, and that its source, a degenerate gland, is not only subcutaneous, but subfascial also, that is, under the deep cervical fascia, and perhaps even submuscular; the communication between the two being by a small opening just large enough to admit a probe, and easy to overlook if it be not carefully sought for. Herein lies the explanation of the chronic sinuses discharging for years, and healing, if they do heal, with a conspicuous depressed scar; or perhaps issuing in subcutaneous burrowings lined by ill-favoured granulations, or an open indolent sore healing at last with a cheloid deformity.

We learn, in the third place, that suppuration of long standing may be brought to an end in the course of a very few weeks if the source of it be recognised and vigorously attacked.

We learn, in the fourth place, that the mark left by prompt surgical interference is not deforming, scarcely dimpled, and is utterly insignificant in comparison with the ugly scar resulting from a sinus allowed to heal at its own leisure after discharging, it may be, for months or years.

Another illustrative case was sent to me in October 1877. Mr. S——, of K——, aged twenty-seven, having been advised to winter abroad on account of symptoms of early disease of the lungs, was urged by Dr. Allbutt to have a chronic discharging sinus in the neck surgically attended to before leaving England. For several years he had been subject to enlargement of the cervical glands, for which he had undergone all kinds of medicinal and external (local) treatment, but with no good result. The sinus in the neck was incised and enlarged, and cheesy remnants of degenerate gland tissue were found and scraped out. This sinus, from which, according to his account, there had been a constant discharge for several years, was quite healed in five weeks after the operation. A year later the scar was pale, non-adherent, and scarcely visible. There had been no further enlargement of glands, there was no evidence of disease of lung, and he was in robust health. Can there be any reasonable doubt that in this case the half-decayed gland, with its septic track, was a serious factor in his depraved condition of health; and that, even if it were not the direct cause of his threatening pulmonary disease, it must have proved a serious impediment, if not an absolute bar, to the happy recovery of lung which took place?

A special lesson to be learned from this case is that it lies with the physician to appreciate the vital importance of any infective complication in a patient suffering from, or threatened with, visceral disease; that it is possible for the surgeon quickly to put an end to many sources of chronic poisoning of the system, and so to give fair play to the means of restoring health which are at the command of the physician.

The next case which I shall bring forward is that of Walter Speight, an infirmary patient. He had been operated upon by us nine times during five years, and seemed to have come to the end of his troubles. On the first occasion the gland had suppurated, and was discharging. In all the other operations the glands were removed or scooped out before the skin had given way. In some instances the glands were suppurating; in others, enlarged glands were enucleated before they had broken down So great was the discomfort he had endured, so marked was the relief that he obtained by operation, that as soon as a fresh gland inflamed he came and begged me to remove it.[1] We learn from this case the value of persistency both in patient and surgeon; in the patient, who was not content until every source of discomfort and of deformity had been removed; in the surgeon, who held not his hand as long as work remained to be done. If it be right to remove one degenerating gland, it is right to work on to the logical conclusion, that all compromised glands, if removable, shall be got rid of. The case teaches us also that we need not be deterred from our good work by fear of a deforming scar; and that it is possible, provided the skin be sound, so to remove a gland as to leave a scar that shall be insignificant. In two other instances, the patients being young ladies, such repeated operations have been performed with most gratifying results. Both were most eager to have their encumbrances removed, and they reckoned the mark as nothing compared with the increase in comfort, rapid recovery, and improvement in health which they had experienced.

Again, Miss B., aged eleven, was brought to me in July 1879 with chronic enlargement of the cervical glands following an attack of sore throat, probably caused by bad drains. A sinus connected with the glands had been discharging for six months, and at another point an abscess was making for the surface. Operations were performed on two occasions; on the first the sinus was enlarged and scraped, and the remains of a decayed gland were removed; the wound healed in four weeks. The abscess, still covered by sound skin, was opened at the same time, and the gland in which it originated was dissected out: this wound healed in ten days. At a second operation, a few weeks later, another unbroken suppurating swelling was dealt with in like manner, and the wound healed in three weeks. The result, as reported two years later, is that there is a puckered thickened cicatrix over the situation of the sinus; but that the scars of those gland abscesses which were not allowed to open spontaneously, were linear and fading in colour.

The lesson here taught is clear—that, apart from the question of ill-health dependent upon the presence of long-continued discharge from a sinus or gland, it is of supreme importance in the matter of scar that the offending gland or pus should be eradicated whilst the skin is sound, that is, before the skin has been damaged by inflammation and thinning; and, above all things, that we should anticipate the formation of a sinus which, by the contraction of its cicatricial lining, draws to a pucker the scar in the skin.

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[1] This man is still living and at work. He has had about sixteen operations by myself and others, including fistula in ano, and removal of inguinal and axillary glands.—T. P. T., Oct. 1896.

Now there are two aspects of the question, both of which must be kept steadily in view—the pathological and the æsthetic. Our guiding principle must be, in the words of Professor Allbutt, "that, whenever septic material is contained in the system, we rest not until it is expelled, and its burrows are laid open and disinfected." In doing this the surgeon must make it an artistic study to effect his purpose with the smallest possible amount of blemish. The ugly scars and unseemly depressions, once so familiar in scrofulous necks, should be deemed an opprobrium of surgery; whilst to delay operation until the skin is thin, red, and ready to break down, or has already given way, should be looked upon as mischievous trifling. May we not hope, moreover, that the time is not far distant when the absolute inutility of painting the skin in the hope of influencing a caseating gland, perhaps deeply seated beneath muscle and deep fascia, and the injury which may be done by this practice to the skin itself, will be fully brought home to the professional mind? The æsthetic question may be stated in the following propositions:—

(*a*) Whenever fluid—that is, pus—can be detected in connection with a diseased lymphatic gland, the operation should be done before the skin becomes red and thin; that is, before the skin has been spoiled by advancing suppuration.

(*b*) When the diseased gland is subcutaneous—that is, not beneath the deep fascia or muscle—and has been completely removed, the least scar will result if neither stitches nor drainage-tube be used; especially if it be possible to leave the wound uncovered by dressing and exposed to the air so that the edges may be drawn and glued together by drying lymph.

(*c*) If the diseased gland be beneath the muscle or muscular fascia, then a drainage-tube must be used, or a temporary drain of cyanide gauze, and the edges of the wound united by suture. For this purpose probably horse-hair or silkworm gut well soaked in carbolic lotion are the best sutures. The best tube for prolonged drainage is a specially selected gilt spiral wire, as it may have to remain from two to eight or ten weeks, according to the depth of the wound, or the completeness of the removal of the gland.

(*d*) Where many glands have to be removed it is better, so far as may be, to remove them through a series of small incisions, and thereby to avoid very extensive ones.

On the "pathological aspects" the following points are worthy of attention:—

(*e*) That all sinuses and suppurating cavities should be thoroughly cleansed by means of scraper or lint, so as to leave a fresh surface free from granulation or decayed or decaying tissues; and that a drainage outlet should be maintained until all the deep parts are healed.

(*f*) It is essential to bear in mind, as I have said, that the visible abscess, which has often been called a suppurating gland, and treated as such, is frequently but a subcutaneous reservoir of pus, the source of which (a degenerate gland) may be not subcutaneous but subfascial; that is, under the deep cervical fascia, and often submuscular, under the sterno-mastoid: the communication between the two being a small opening in the deep fascia just large enough to admit a probe or director. This opening may readily be overlooked, and is not always easily found even when searched for, but it must be found, or the operation will be a failure.

This opening is often more easily detected by the touch than by a probe or director. After thoroughly cleansing the cavity the finger should search the whole bottom of it, and will often detect a slight depression, or the bare suspicion of a depression.

On introducing a director into the depression it is found that the director travels more deeply, and on withdrawal brings in its groove a little pus or caseous matter from a deeply-seated broken-down gland Such an opening may be cautiously enlarged by the knife, or, if necessary, by a Bigelow's dilator, until the finger can test the new cavity in its turn, and decide whether the end has been reached or not. The education of my finger in the detection of this "critical pit" has recently proved of great service to me when dealing with two cases of abscess at the upper part of the thigh, enabling me after careful search to detect the very small opening near Poupart's ligament which led to the source of the pus · in one instance it was near the cæcum, in the other near the kidney; neither of the cavities, so far as I could make out, extending farther, or being connected with disease of the spine.

(*g*) As it is mere trifling and bad surgery simply to incise an abscess in the neck without searching for and thoroughly eradicating the gland that is the starting-point of the abscess, no such abscess should be opened without putting the patient under ether, and being prepared with all necessary means for eradicating the diseased gland.

(*h*) It sometimes happens that after the extirpation or evisceration of a gland, the finger detects in the wall of the capsular cavity the slight convex bulging of a contiguous gland. This should be pricked through the wall of the cavity, and so reached and extirpated or eviscerated. In this way in several instances I have emptied from one external opening a group of three or four glands, massed together and suppurating, or otherwise broken down.

(*i*) What has been said hitherto concerns glands which are suppurating or obviously breaking down. As to caseous glands the conclusions I have arrived at are as follows:—When we have dealt with a broken-down gland which has proved to be undergoing caseous degeneration, we may infer that any other enlarged glands, then present or subsequently appearing, are becoming caseous also; in my opinion, therefore, it tends to promote better health of the patient if, in the absence of reason to the contrary, such glands are removed as soon as the surgeon is convinced that the enlargement is persistent and not merely transitory, without waiting for evidence of fluctuation or pus.

(*j*) What shall be done with enlarged glands which are neither caseous nor suppurating; glands indicated by the names lymphadenoma, hypertrophy, and so forth? I am not clear as to the answer to be given, nor whether their removal is an advantage or otherwise. Probably this question will remain open for some little time to come [*vide* p. 593].

(*k*) In a very large number, indeed in a majority of the instances of scrofulous neck which have come under my care, there was no evidence of any constitutional taint or weakness. The origin of the ailment was often clear and defined, bad drains in many instances, scarlet fever, mumps, tubercle of the tonsil, and the like in others. The cases were frequently isolated instances in families free from any tendency to constitutional disease, and health and perfect vigour were restored after the destruction of all degenerate or infective material.

There are two more points of surgical practice on which a word should be said. The first is on the use of large incisions, combined with division of the sterno-mastoid, enabling the surgeon to see and dissect away deeply-seated glands. The testimony of those who advocate such incisions is that the eradication of the diseased glands is thereby rendered very effective and comparatively easy. Perhaps I have not met with disease of deep glands extensive enough to call for these large incisions, my experience, of late years, having been amongst people above the poorest classes. At any rate I have not employed them, and I have divided the sterno-mastoid in but a few cases, and in these only partially. I am therefore unable to state from my own experience whether the scar resulting from the more extensive operation is such as would lead me to restrict the employment of the large incisions to the very extreme cases only. To form a judgment on such a point would need the comparison of a series of cases of each kind after the lapse of two or three years from the time of the operation.

The second point is the bold suggestion of Mr. Watson Cheyne, that in dealing with large masses of glands adherent to the sheath of the cervical vessels, the whole of the underlying internal jugular vein should be removed. Here, again, it may be that I have not met with the extreme cases in which such a course would be advisable. On one occasion, in stripping a gland adherent to the sheath, I tore open the internal jugular vein, much to my dismay. I tied the vein above and below, and divided it between the two ligatures, and the wound gave me no more anxiety. It is important to know from the experience of Mr. Cheyne, and of Mr. H. J. Stiles, who has adopted the same plan, with what impunity such a step may be taken. Indeed, it would seem to be a point gained in recent surgical procedure, although the need for adopting it may be very rare.

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REFERENCES

1. Allbutt, T. Clifford. "On the Treatment of Scrofulous Glands," *Trans Internat. Med. Congress*, 1881, vol. ii. p. 82.—2. *Idem.* "On Scrofulous Neck," *Med. Times and Gazette*, Jan. 3, 1885.—3. Allbutt and Teale. *On Scrofulous Neck*, and *On the Surgery of Scrofulous Glands.* London, 1885.—4. Cheyne, Watson. *Treatment of Wounds, Ulcers, and Abscesses.* 1894.—5. *Idem.* *King's College Hospital Reports*, vol. i.—6. Renton, Crawford. "Treatment of Tuberculous Glands," *Brit. Med. Journ.* Sept. 12, 1896.—7. Stiles, Harold J. *Ibid.*—8 Teale, T. Pridgin. "On the Surgery of Scrofulous Glands," *Med. Times and Gazette*, Jan. 10, 1885.—9. Treves, Frederick. "On the Pathology of Scrofulous Lymphatic Glands," *Brit. Med. Journ.* April 30, 1881.—10. *Idem.* *Scrofula and its Gland Diseases.* 1882.

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OBESITY

Introduction.—Obesity—sometimes, but improperly called polysarcia, a name introduced by Cœlius Aurelianus in the sixth century—may be defined as a condition in which, owing to one cause or another, an overgrowth of fat takes place in many parts of the body. The nosological position of this state is rightly assigned amongst the several hypertrophies. The body in health is more or less covered with fatty tissue, and certain parts are well clad, both without and within. Improved nutrition of the whole body increases the fat, and diminished nutrition is rapidly indicated by a loss of it. We are only concerned now to take note of such adipose overgrowth as constitutes an unwholesome or morbid state, leading to undue bulk, disproportionate body-weight, and interference with due performance of various functions. "Le développement de la grasse ne constitue une maladie que lorsqu'elle entrave le jeu d'un organe quelconque" (P. Legendre).

In this case we have to deal with a definite tissue-proclivity, which, as in other instances, may be either inherited or acquired. A family tendency to obesity is well recognised; but the several members of such a family may not all become the subjects of it. Mode of life has much to do in determining the occurrence of obesity, and thus singular unlikeness may exist amongst the individuals of a predisposed stock. Such a tendency may be noted in certain members of a family inheriting the arthritic diathesis; gout or glycosuria, for example, occurring in some members, and an extraordinary obesity in others.

The sexual relations of pinguesence are noteworthy, and must be considered in taking a complete view of the subject. Adipose development is as normal a mode of nutrition at puberty in the woman as is the development of the breasts and ovaries. In this connection we note also the increased tendency to fatty deposition which is apt to ensue on the removal of the testes in male animals, and of the ovaries in the female. Towards the age of forty years the same tendency is to be noted in both sexes—the change in such cases being partly due to diminished bodily activity and the easier life not seldom enjoyed at this period.

Undue obesity is, as a rule, no indication of soundness or robustness of constitution. In infancy an excess of fat is not a sign of general good nutrition. Thus, a child may be at once very rickety and very fat; and the latter state is apt to deceive the unwary as to the serious underlying condition. In hysterical girls there may be noteworthy obesity in spite of a miserable appetite and a very small supply of food. The breasts may become very fat in women the subjects of amenorrhœa; and the condition subsides on re-establishment of the menses. Atrophy of the testicles has been known to be associated with inordinate growth of mammary fat in males. The sexual appetite is distinctly lowered in obese persons; and inertness of the sexual organs certainly favours the deposit of fat.

Lean and elderly spinsters not infrequently grow plump after marriage. As pointed out by Sir James Paget, after the age of forty years persons either diverge into spareness or become more or less obese; the former, as a rule, enjoy the happier and longer lease of life.

Heredity apart, the conditions which determine obesity in a morbid degree are diet, exercise, and habits of life. In cases presenting a strong hereditary tendency to fatty hypertrophy, habits of diet count for less, and the proclivity may be little influenced by measures which prove effective in other cases.

We are not now concerned to discuss cases of local overgrowths of fat or fatty tumours. These may be single or multiple, of slow or of rapid growth. Such tumours are commonly hereditary, as much so as are atheromatous cysts or wens. Habits have little, if anything, to do with these. Two exceptions may, however, be mentioned: first, cases in which local irritation, long continued, induces a fatty growth; and, secondly, cases of symmetrical fatty tumours (lipoma), above the occipital region, due to excessive beer-drinking, described by the late Mr. Morrant Baker: of these I have seen a good many examples.

We may also note some racial peculiarities in respect of obesity. The peculiar gluteal development of the Hottentot women deserves mention, and the common tendency to obesity in the Hebrew race is remarkable. A singular contrast is to be observed between the Teutonic races and the people of the United States of America. The former often present examples of obesity; the latter, although largely recruited from the former, exhibit markedly less tendency to this condition amidst the environments of the New World. Climate may have to do with this result; but habits and diet are probably much more concerned in it. In the East remarkable examples of obesity are met with, but amongst Hindus rather than Mohammedans. Customs and diet account for this difference; and European indulgences, including alcoholic habits, united with Oriental indolence, not seldom afford the explanation of these anomalies.

In a moderately fat man the fat has been estimated at one-eighteenth or one-twentieth of the total body-weight; and in woman the relative proportion is larger. It is naturally found in the face, in the orbits, palms of the hands, soles of the feet, flexures of joints, around the kidneys (suet), in the mesentery and omentum, in the appendices epiploicæ, the subcutaneous areolar tissue; in certain situations, such as the abdominal wall, mammary region, and in the cancellous and canalicular tissue of bones, especially in yellow marrow. No fat is met with on the scrotum or penis, or on the nymphæ; nor is there any between the rectum and bladder. None is found within the cranium.

In the viscera fat is normally met with in the intimate cells of the liver, and in the cells and tubules of the brain and nerves.

The sources of fat in the system are dependent on the supply of food; fatty matters reach the blood from both animal and vegetable pabulum, but especially from non-nitrogenised materials, such as starch, sugar, gum, and alcohol. Fat itself affords an immediate supply; but only a small portion of the stored fat in the body comes directly from that consumed with the food. Excessive pinguescence is normally kept in check by the means which induce full oxygenation of the blood and tissues. Hence, if organic compounds rich in carbon are fully supplied, and oxygen but inadequately, favouring conditions exist for fatty deposition. Diminished exercise and close confinement lessen oxygenation by preventing the dissipation of carbon compounds. These facts are well illustrated by the results of captivity on animals, and by examples only too common in the social systems of the human family; and they afford a clue at once to the nature of the proper remedial measures.

As pathologists and clinical observers we have to distinguish, as far as we can, between fattiness due to infiltration and that due to degeneration. In the former case infiltration (lipomatosis) should be regarded as an excessive deposition in the cells which normally contain fat, as in the subcutaneous areolar tissue, omentum, perinephric region, liver, and parts between muscular fasciculi in the voluntary and cardiac muscles. Such an infiltration, though general, may in certain parts be in excess; it is then met with, especially in the abdomen and in the integuments about the mammary region and the buttocks.

In the heart, infiltration is common, and is not inconsistent with vigorous action of this organ. The visceral layer of the pericardium is a common seat of it; so also is the interstitial connective tissue. This is not to be regarded as an example of "fatty heart," since the muscular (sarcous) elements may be quite healthy in such a case. Obese persons may have abundant fatty accumulation amongst their muscular bundles, and such muscles, though hampered and weak, may be sufficiently sound to resume full function if they be relieved of their fatty encumbrance. Obesity tends to induce inaction and muscular inability, and so there is a vicious circle of malign events in such instances.

The liver becomes fatty under similar conditions, as where persons eat fatty food or much carbohydrate material; and especially if they are immoderate in alcoholic fluids, which combine more readily with oxygen than does fat.

Fatty degeneration is a more serious matter. In this case fat is found in the tissue-elements themselves, as in the sarcous particles of muscle or the walls of blood-vessels; and it is not necessarily introduced by the blood. Decay of structure is in progress here as a result of a malign metabolism, albuminates being broken down into fat; a process which has been likened to that occurring in the "ripening" of cheese, where fat is formed at the expense of albumin. Arcus senilis, cataract of the lens, and fatty change in small arteries are good examples of fatty degeneration; and the truly "fatty heart," in which the sarcous elements change into fat drops, is an exquisite one.

We are only concerned here to consider fatty deposit and infiltration in excess; it falls to others to describe the lesions and the effects induced by fatty decay or transformation [*vide* vol. i. p. 185].

Fat is apt to be deposited in excess after anæmia due to repeated hæmorrhages or otherwise; and is commonly met with in chlorotic young women. Deficiency of hæmoglobin in the red globules of the blood entails insufficient supply of oxygen, and thus leads to storage of fat. In Addison's disease the fat remains. In wasting disease fat is lost early; and in cases of inanition it is observed to disappear early from the face, giving rise to a characteristic starved and gaunt aspect.

Fat is often fluctuating in quantity; much of it may disappear in a very short time, and no less rapidly may it be again deposited. Human and animal fat contains olein or liquid fat, and stearin or palmitin which are solid fats. The sources of it, as already stated, are from various articles of diet, and an ordinary dietary contains from one to two and a half ounces of fat. Carbohydrates, such as starch and sugar, especially tend to produce it. It is probable that fat can be also converted into carbohydrates, such as dextrose, its carbon being thus transformed for use in the tissues as a soluble and readily diffusible carbohydrate. This may conceivably occur when the body has to draw upon its own store of fat and so lose its undue corpulence.

Albuminous matters are certainly capable of transformation into fat. Some of these, after conversion into peptones by the stomach and pancreas, pass under pancreatic influence into leucin, a fatty body. The ferments of the salivary glands and pancreas convert starch into sugar; but the method of conversion of sugar into fat is not yet precisely ascertained. The fats are partly saponified and partly emulsionised by the pancreatic and other secretions. This secures a very fine molecular division of them, so that absorption may readily proceed, by means of the epithelium of the villi, into their lymph-spaces, and so reach the lacteals, mesenteric lymph-glands, and the thoracic duct.

Normal blood contains about one-half per cent of fat, the muscles more than three per cent, the brain eight per cent, and the nerves twenty-two per cent. The nerves are the last to lose their fat in cases of general atrophy, and the large amount normally present in them is significant of [illegible] importance of fat to their well-being and potential activity.

The amount of fat in the blood may be readily increased by certain articles of food—mostly by fat, sugar, and starchy matters; in less degree by animal food, and least of all by bread.

Fat is a bad conductor of heat. Warmth is retained in the body by the panniculus adiposus, and the intestines are especially protected by the fat in the omentum and appendices epiploicæ. Hence the stout require less warm clothing than lean persons; and the latter suffer more readily from chills and exposure. Normal radiation of heat is checked in the obese.

It is not sufficiently recognised that fat deposits are constantly undergoing change by decomposition and reformation. As with all other tissues, intimate change proceeds even in the densest layers of fat; and in no part of the body does any fatty deposit lie out of the current of life and unaltered.

That the proteids possibly constitute a source of fat is proved by the fact that while the urea which is excreted represents all the nitrogen which is thus passed through the body, it represents much less carbon than is found in a quantity of the proteid yielding the same amount of nitrogen. This surplus of carbon, if not otherwise disposed of, remains as a possible source of fat to be deposited in the body. It has been calculated that thus 100 grms. of proteid food might furnish 42 grms. of fat (M. Foster).

I have said that heredity has largely to do with the occurrence of obesity; according to Oertel of Munich this influence can be traced in 50 per cent of all cases. We have, then, to deal with a very definite diathetic condition in which a special trophic process is at work—one as definite in its course and outcome as in that in which a gouty or a strumous disposition prevails. It is of high importance to realise this fact, and, if possible, to come to some clear understanding of it before undertaking a line of treatment for any obese person; for a marked difference is to be noted between cases in which obesity is the outcome of heredity and those in which the encumbrance is acquired by certain habits and modes of life. Where hereditary disposition is potent and effective we are less hopeful by far of good and lasting results from any plan of treatment. When the disorder is acquired by bad habits, improper diet, and indolence, we may readily modify it; and, in patients who co-operate intelligently and honestly, we may largely and permanently dissipate the fatty encumbrance. The mental peculiarities and temperament are deeply concerned in every case; the difficulties of treatment are greatly enhanced in persons of indolent and phlegmatic habit, and proportionately diminished in persons of active and energetic disposition.

The relation between gout and obesity is one of much interest. Gout figures largely in many cases. It is not unusual for certain members of a family with gouty inheritance to become obese. This may occur in either sex and sometimes before puberty. After the age of thirty obesity may set in, and within ten or fifteen years glycosuria. Such persons belong to the class of fat or gouty diabetics, and in them the glycosuria is but a mild form of chronic diabetes. The presence of glucose in the urine is almost the only symptom which such patients have in common with those who are the subjects of the graver disorder. They often have no thirst and but little polyuria, and for many years they lose very little weight. These are the patients who gain much benefit from recourse to spas, and the disorder may be arrested sometimes, or become intermittent. Carefully regulated dietary may occasionally remove all glucose from the urine, or a small percentage of it may persist.

If neglected, such cases may drift into incurable forms of diabetes, with thirst, polyuria, wasting, poor health, and great vulnerability of texture. Pulmonary tuberculosis, furunculosis, or gangrene of the extremities usually terminates life. Diabetic coma is not a very frequent mode of death in these cases. Such patients may live for fifteen or twenty years, or even longer; and occasionally present acute or chronic phases of gout in some of the joints, with temporary alleviation or removal of the glycosuric state. Such cases are peculiar, and especially striking when met with in families where other members may be either spare or more overtly gouty; or exhibit other features of gouty inheritance, such as hemicrania, biliary calculi, or mere lithiasis. Here we may note again the strong hereditary tendency both to obesity and to glycosuria in the Hebrew race. I shall return to the discussion of these cases when considering the appropriate treatment of obesity. A moderate degree of obesity in early life may disappear during adolescence and never recur.

Two leading kinds of obesity are met with in practice, and may be classed as (A) the plethoric, and (B) the anæmic. The former prevails more in men, the latter in women.

A. The plethoric kind.—In this kind there is a general over-nutrition, the muscles are large and well developed, and the blood rich in red globules and hæmoglobin. The heart hypertrophies and acts at first with vigour, but subsequently it dilates and loses power. The pulse becomes infrequent and of high pressure. Arterial sclerosis is set up, and the vessels become tortuous. As in ordinary cases of heart disease associated with much vascular peripheral resistance, circulatory troubles gradually ensue in the lungs and other organs. Albumin may appear in the urine. Anginal attacks may supervene, and progressive dropsy. Cardiac asthma sometimes occurs, especially at night. The respiration in the later stages may assume the Cheyne-Stokes form. Cerebral hyperæmia, indicated by throbbing of the carotids, vertigo, and tinnitus aurium, is not uncommon epistaxis may relieve it. Rupture of an artery in the brain may occur on a sudden increase of intravascular pressure; and in such cases this event is commonly fatal. As cardiac failure progresses arterial pressure falls, and the pulse becomes intermittent or dicrotous.

B. The anæmic kind is characterised mainly by an associated impoverishment of the blood: cases of the plethoric kind may eventually present hydræmic conditions and fall into this category. The obesity may be extreme; but the fatty masses are flabby, and the muscles are ill-developed and feeble. The heart partakes of this muscular inadequacy and acts feebly, the pulse being small. Some elevation of arterial pressure, due to peripheral resistance, may, however, be met with as in ordinary cases of anæmia. In short, we have all the prominent features of anæmia, together with excessive fatty deposition: great incapacity for exertion, ready induction of palpitation and dyspnœa, and small appetite. These patients are neither gross feeders nor always large drinkers. They have often, indeed, an aversion from animal food, and prefer a dietary rich in carbohydrates. The deficiency of hæmoglobin in the blood and the consequent inadequate oxygenation maintain and increase the tendency to obesity. As already stated, women are the common subjects of anæmic obesity; and the disorder may be manifested before full growth of the body is established, namely, before the age of twenty-two. Menstruation is generally disordered, or may be absent. Menorrhagia, or losses of blood after child-bearing, may lead subsequently to anæmia and to obesity.

This variety is sometimes met with in men after exhausting illnesses, and is not infrequent after enteric fever, acute rheumatism, or pneumonia. It is also witnessed after submission to full mercurial courses for the purpose of eradicating venereal taint; but it is not met with in cases of operatives suffering from hydrargyria.

Dropsy is commonly associated with anæmic obesity. The arterial pressure falls at last, the flow of urine becomes scanty, and, in spite of free perspiration, the tissues become water-logged.

Such patients are altogether more seriously ill than those of the plethoric kind, since the latter may bear with their condition for many years before the blood becomes impoverished and hydræmia sets in. The muscular debility is a factor of supreme importance in the former cases, and adds to the difficulties of successful treatment of the symptoms.

Whether anæmic or plethoric, the subjects of obesity are ill adapted to bear the inroad of acute diseases. Fever, in particular, is very badly borne by them: fatty investment interferes seriously with the dissipation of the heat generated in the body, and thus there is in these cases a special tendency to hyperpyrexia to an amount incompatible with life. Acute fevers and pneumonia are therefore very dangerous maladies for obese persons. Antipyretic measures are seldom effective; and drugs such as quinine, antipyrin, and salicylates are badly borne, and may induce collapse. Cold baths in cases fit for it are more successful. If life be saved, convalescence is tardy; and an increase in obesity may occur in response to the necessary supporting alimentation. This is due to the inherent vicious metabolism which pertains to the trophic habits of such patients.

The line of progressive failure in all these cases may be traced into almost every system of the body. Heart failure and arterial sclerosis have already been referred to. The lungs become the seat of bronchial catarrh, and emphysema may supervene. Gastro-enteric catarrh and gastrectasia from over-eating and drinking may prove troublesome complications. A gouty tendency may lead to lithiasis and to the formation of stone in the kidney. The latter disposition has long been recognised as an appanage of the obese. The liver becomes fatty and greatly enlarged, adding much to the general discomfort and to respiratory incapacity. Gall-stones may form in the gall-bladder, and biliary colic occur. The skin becomes unctuous, and comedones and flat greasy warts may be formed. Eczema, erythema intertrigo, and furuncles are not infrequent; and if alcohol be freely taken, gutta rosacea and hypertrophy of the nose may be present. The causes of death in cases of obesity are syncope, cerebral apoplexy (from degenerate arteries), cardiac rupture, angina pectoris, and uræmia.

Due consideration of the foregoing facts should convince any careful practitioner of the futility of treating obese persons by any uniform method. In these cases, as in all cases of disease, regard must be had to the individual and to the personal factors present; and the particular nature of the obesity must be accurately discriminated before any therapeutic measures are attempted. The question of inheritance or of acquirement must be settled, and the patient, and not his symptoms merely, must be treated. Without doubt much harm may be done if a hard and fast line of treatment be indifferently instituted. In this way it is that patients, to reduce their obesity, are sometimes set to pursue dietetic and other measures which may prove not only unavailing but positively mischievous; and others venture to carry out vaunted methods on their own responsibility, not seldom with risks to their general health, which, if unrecognised, are none the less grave.

We must understand, in the first instance, that obesity may be little more than the normal trophic equilibrium for a certain person; and any efforts, seriously pushed, to alter this special conformation may be fraught with risk to his general well-being. As Dr. Michael Foster says: "The same tissue has in different races and different individuals specific and individual characters of nutrition. The flesh of the dog is not the same as that of a man, the muscle of one man lives differently from that of another."

On the other hand, to quote the words of Sir James Paget, "the over-fat are certainly a bad class, especially when the fatness is not hereditary, but may be referred in any degree to their over-eating, soaking, indolence, and defective excretions. The worst of this class are such as have loose, flabby, and yellow fat; and I think you may know them by their bellies being pendulous and more prominent than even their thick subcutaneous fat accounts for; for this shape tells of thick omental fat, and I suppose of defective portal circulation. I know no operations in which I more nearly despair of doing good than in those for umbilical hernia or for compound fractures in people that are over-fat after this fashion. Nothing short of the clearest evidence of necessity or of great probable good should lead you to advise cutting operations in people of this kind. Do lithotrity for them rather than lithotomy determine very carefully whether it is absolutely advisable, that you should do either; incline against amputations for even bad compound fractures, and, whenever you can,—as, for instance, for cutaneous cysts, hæmorrhoids, and the smaller examples of scirrhous mammary cancers,—use caustics rather than the knife or ligature."

Hence it is that I strongly urge that the conduct of all such cases should be conducted by the clinical skill and under the constant supervision of a well-trained medical practitioner. This much being conceded, it is not too much to affirm, further, that there is nothing special or peculiar in the subject of obesity which any well-educated medical man may not be trusted to deal with. It is necessary to assert this much, because of late years this matter has been absurdly exalted into a "speciality"—a pretension unworthy of our profession and misleading to the general public.

Obesity is recognised by medical officers for life-assurance as an indication of imperfect health. If the body-weight bear an undue proportion to the height of the individual, such cases are either "loaded" or declined as second or third class lives. Obese persons bear accidents badly, are unsatisfactory subjects, as we have seen, for surgical operations, and are apt to succumb to serious illnesses. Adults of medium height and fair symmetry, who weigh over fifteen stones, may be considered moderately obese. A weight of twenty stones and over constitutes a grave case; but examples are on record where weights of over thirty stones were scaled. Daniel Lambert weighed thirty-two stones at the age of twenty-three, and reached fifty-two stones and eleven pounds in later years.

Occupation and habits of life are familiarly known to induce obesity in certain classes of persons. Sedentary life, whether in or out of doors, favours it. Active members of any profession are not prone to become corpulent unless there be a strongly-inherited tendency. Coachmen are apt to suffer unless they groom their horses. Soldiers and sailors do not become obese until they retire from active duties. Sea-captains, owing to their good appetites and limited locomotion, are often victims in spite of their open-air life. In all these cases habits of beer-drinking or of spirit-drinking (even if well diluted) are certain to aggravate the tendency. Cases of extreme obesity may be noted amongst monks, whose duties do not entail much muscular activity; and who, if they eat little meat, often partake largely of fats and carbohydrate matter. Mental activity, worry, and anxiety all tell against obesity, and so do grief and the irritable or nervous temperament.

Treatment.—*Preventive.*—The main indications are to secure habits of strict temperance in respect of food and drinks, and to ensure a life of activity, both mental and bodily. This is especially important when a hereditary tendency to corpulence is present; and it applies to young children and young adults no less than to persons in the third or fourth decades of life. An obese mother is a bad nurse for her infant; a good wet-nurse will be better. If the latter cannot be secured the mother should be dieted, and fatty and carbohydrate foods be restricted as far as possible. Beer should not be taken. Artificial feeding with sterilised cow's milk is probably better than the maternal milk, and farinaceous food should be excluded, or much reduced in amount, malted food being preferable. In early adult life fat-forming food is to be restricted, and abundant muscular exercise in the open air encouraged. Seaside residence is especially favourable and sea-bathing when practicable. Later, active exercises are of much value; and athletic pursuits in moderation, such as gymnastics, tennis-playing, riding, rowing, and swimming, may be enjoined with great advantage.

Dietetic.—Without doubt the most remarkable results in diminishing corpulency due to undue formation and storage of fat in the body are secured by the modification of the ordinary dietary. Modern physiology and chemistry alike indicate the main lines to be followed in this respect. In recent times professional and public attention has been specially devoted to this matter by the successful treatment which was instituted some thirty years ago in the case of Mr. Banting by his medical adviser Mr. Harvey. The essential feature of it consisted in the withdrawal of fat-forming food. Mr. Banting took freely of animal food, but ceased to take bread, butter, milk, sugar, potatoes, and sweet wines. No limit was placed on the amount of water, and from six to eight ounces of light red wine were taken daily. On this system forty-six pounds of weight were lost within a year, and although the patient was sixty-six years of age he recovered a large measure of health and comfort. This plan of treatment, while it secures the absence of food that most readily induces obesity, is also characterised by a very large ingestion of nitrogenous matters which are difficult of complete digestion and assimilation. In other cases in which it was employed it provoked indigestion, and caused depression and various nervous symptoms. The quantity of albumin was partly consumed in the production of heat. This method, then, is unsatisfactory in principle and in practice; partly because of the digestive inadequacy of the body to deal with so much nitrogenous matter, and partly because of the slender value of it as a heat-producer within the organism. The nervous system also suffers from deprivation of fatty matters in such a diet. Fatty food is less liable than carbohydrates to cause obesity, being less easily oxidised, and interfering less with the disposal of albuminous matters. In a given weight it contains more potential energy than the carbohydrates.

Experience has plainly shown that a small proportion both of fat and carbohydrates must be combined with the nitrogenous ingesta in order to ensure normal metabolism; and, to secure a consumption of fat already deposited in the body, muscular exercise must be freely taken to induce increased nitrogenous decomposition. Under these conditions the obese patient loses fat. Muscular activity promotes oxidation of fat, and the small amount consumed in the diet is thus readily disposed of. Carbohydrates are more digestible than fats.

The influence of fluids, more especially of water, upon fatty deposit is probably considerable when large quantities are consumed. The evil effects of diluted alcohol and saccharine matters are well ascertained. In many cases of obesity there is a marked disposition to drink copiously.

The appetite for food is found to be normal in about half the cases, while it is increased in a somewhat smaller number. In some cases the appetite is below the normal.

Restriction of fluid food will certainly assist greatly in reducing corpulence in such cases as may be properly treated in this way.

"Bantingism" then, as a system, is both unphysiological and impracticable. Its failure led Ebstein to recommend a modification of it in which fat was permitted, but starchy and saccharine matters almost withheld. Oertel's system of dietary practically corresponds with this; but he enjoins with it graduated exercise, restriction of fluids and fat, and with measures to fortify the muscular system generally and the cardiac walls in particular. Schweiniger's system is very similar, but he forbids fluids at meal-times, and prescribes them two hours subsequently. The Salisbury treatment consists in a very free allowance of animal food and entire absence of carbohydrates, large quantities of hot water being taken to wash out the excessive nitrogenous metabolic products from the body. In any case particular attention is to be paid to the condition of the heart, with a view to reinforce it as much as possible. The urine no less demands careful attention; when lithates are abundantly thrown down, the amount of nitrogenous food must be diminished. Deficient excretion of urea demands a similar procedure until a fair percentage is passed, when the diet may be altered in this respect. Bouchard recommends fruit and fresh vegetables, that contain potass salts, to encourage a more free oxidation of carbohydrates in the diet.

Weir Mitchell and Bouchard recommend a dietary of milk and eggs, and the exclusion of all other food. Thus, for three weeks they prescribe half a pint of milk and an egg every three hours five or six times in the twenty-four hours. At the end of this period they vary the diet in accordance with the general principles just mentioned. The proper ratio between the nitrogenous and carbonaceous elements is fairly maintained by this early treatment. Constipation is likely to occur, and the patient is unfit for much exertion. The monotony of this diet may prove hard to enforce in patients of feeble purpose.

The general principles to be observed in treating cases of obesity relate, then, so far as dietetic measures are concerned, to the restriction of fats and carbohydrates, and no less to a certain increase in the proteids. The latter augment the metabolism of the whole body.

Of food-stuffs a healthy adult requires—of proteids 100 to 130 grms., fats 40 to 80 grms., carbohydrates 450 to 550 grms., salts 30 grms., and water 2800 grms. The carbohydrates should thus be four or five times in excess of the proteids. Experience shows that all these elements are necessary for perfect nutrition, fatty matters in particular. The fats and carbohydrates, though chemically allied, are subjected to divergent metabolism, and are not mutually interchangeable without risk to the economy. The carbohydrates are believed to supply heat more rapidly than fats —the latter requiring more time to afford this form of energy, having probably first to be converted into sugar. Both in health and disease, it is to be borne in mind that no isolated organic principle is by itself capable of supporting life. Instinct and knowledge prove alike that there must be a combination of principles furnished to the system for due nutrition.

In treating cases of obesity the patient should be accurately weighed. A careful physical examination of all the organs and secretions of the body should be made, especial attention being paid to the condition of the muscular walls of the heart, the state of the arteries, and the urine. The question as to heredity or acquirement must be noted; the temperament, and the habits of life in respect of food, exercise, and occupation, the age and sex, and the form of the disorder, whether plethoric or anæmic, are to be considered. An inquiry as to gouty proclivity or to hæmorrhagic tendency is necessary. The presence of glucose in the urine demands careful attention, and its significance must be gauged as far as possible. Any indication of renal insufficiency, as evinced by a persistently deficient output of urea, is particularly to be noted; because this condition plainly demonstrates the unfitness of the patient to bear a dietary rich in proteids.

Two objects are to be sought in treating any case: *first, to reduce excess of fatty deposits; secondly, to prevent reaccumulation of it.* The first is often more or less easy, but the second is often rendered difficult by restiveness and want of due control on the part of the patient.

The following *dietary* may be usefully enjoined in many cases:—Six or eight ounces of hot or cold water may be taken half an hour before breakfast. Breakfast should consist of one or two ounces of well-toasted stale bread without butter, grilled white fish, grilled mutton chop or beefsteak, or cold chicken, game, beef, tongue, or lean ham. One or two small cups of tea or coffee, with a little skimmed milk and without sugar, may be taken. Saccharine may be used as a sweet-flavouring agent, but is commonly disliked. Six ounces of bouillon or clear soup may be taken by weakly patients between breakfast and luncheon, and a gluten or almond biscuit with it. For luncheon order cold meat, or a poached egg with spinach or lettuce, or other green vegetable, as water-cress and mustard and cress, or a small omelette. Crust of bread or hard biscuit in small amount is allowable, and a small quantity of fresh butter. A glass of good Bordeaux or Moselle wine (dry) may be taken with as much water. A cup of tea, with a little skimmed milk and a rusk or gluten biscuit, may be taken in the afternoon. For dinner, no soup is to be taken as a rule, but occasionally about eight ounces of a thin consommé may be allowed; then a little grilled or boiled fish, without starchy or fatty sauces, but flavoured sometimes with anchovy or some other sauce, oysters, or caviar, a little grilled or roasted meat, mutton, game, or fowl, with a small proportion of fat, green vegetables, no potatoes, and some stewed fruit flavoured with saccharine, or made less tart by the addition of half a teaspoonful of Rochelle salt. Two glasses of claret or of a dry Moselle diluted with water are allowable. Later in the evening a cup of hot weak tea without milk, or as much hot water, should be taken.

Such a dietary, adapted for an adult man, is little irksome to any serious patient. It should be continued for some weeks. Women will naturally require smaller quantities of each article. Exercise of any kind is most desirable between meals, and life in the open air is to be carried out as far as possible. Seven hours' sleep is commonly sufficient, and no sleep should be sought except in bed. The patient should lie on a hair mattress and in a well-aired room. Tepid bathing and a cold shower bath on rising, with good subsequent friction, should be employed daily. Alcohol in the form of diluted brandy or whisky is unadvisable.

Accordingly as weight is lost, the general health being good in all respects, this dietary may be varied with suitable precautions, and a more or less strict attention be paid to the various details of it. If the treatment succeed, increased capacity for exercise, brain-work, and a general sense of relief and comfort, perhaps long unfelt and enjoyed, will be experienced. The action of the heart should become more vigorous, the pulse fuller and firmer, the expiration easy, and the urine remain clear on cooling. Tobacco-smoking should be restricted, and used only after meals. The bowels must be relieved daily; if constipated, moved by two drachms of Carlsbad or Homburg salts, or by a dose of white mixture (haustus albus) while dressing in the morning. If digestion is languid or uncomfortable, a mixture containing dilute nitro-hydrochloric acid and nux vomica, or chiretta, may be taken in the forenoon and afternoon before meals.

Cases of anæmic obesity require iron in some form, and the scaly preparations of it are perhaps the most serviceable, given in calumba or quassia infusion.

If fatty accumulation is found to recur with relaxation of the enjoined dietary, either in its quantity or quality, stricter measures will be indicated with a view to maintain as good general health as possible, and also to control the persistent tendency to pinguescence. One article after another in the diet must be left out till a fair balance of nutrition is permanently secured. For an adult in early and middle life the relative quantities of food required should average 12 to 14 ounces of meat, 6 to 8 ounces of toasted bread, rusk, or gluten and almond biscuit, 4 to 5 ounces of green vegetable, 1 to 1½ ounce of butter and fat, and 30 to 35 ounces of fluid, including wine, tea, and water. As a disciplinary measure it is proper to measure and weigh the food at the outset of treatment. This method also prevents an insidious tendency to excess in some articles of the dietary. The patient should be weighed, in the same clothing, or better still without clothes, once a week.

Treatment by diminution of fluids (*dry diet*).—It is certain that the weight of the body and over-storage of fat can be reduced more or less by a reduction in the amount of fluid consumed. To take an example: I treated a hospital out-patient some years ago, a woman under forty years of age, presenting the plethoric type of obesity, who weighed twenty-one stones, with a dietary in which white bread, potatoes, and sugar were largely reduced, but not excluded, and the consumption of fluids of all sorts limited to thirty ounces per diem. The patient was an intelligent and trustworthy person. She often took less than the prescribed amount of fluid. For medicine I ordered some dilute nitro-hydrochloric acid and nux vomica. Within eight months there was a loss of between seven and eight stones, the diet being maintained; and no increase in corpulency took place for another year or longer while the patient was under observation. The general health and comfort secured were very noteworthy.

One may not always succeed so well; but in restricting liquids, as in limiting anything else, there is often great difficulty in securing co-operation and obedience from patients accustomed to self-indulgence, especially if treatment be carried on at home.

The plan of restricting fluids may be applied in any case of obesity presenting no contrary indications. In cases with weakness and dilatation of the cardiac walls, where hydræmia and tendency to dropsy exist, as in the anæmic type of cases, the benefit from a so-called "dry diet" may be very marked. It is well to limit the fluids of all kinds to thirty ounces, but the amount must vary a little according to the time of year and the particular food taken. Cardiac tonics, such as digitalis, are found to act with more efficiency when restriction of fluids is practised.

This plan is not practicable nor advisable in cases in which glycosuria is present. It may be noted that obesity may long precede the occurrence of glycosuria, and that early treatment for the former may not improbably stave off the latter condition.

Increased water-drinking sometimes necessary.—More free dilution, especially by water-drinking, is advisable, and indeed necessary, to remove excess of glucose from the system. Not less than three pints per diem may be considered the normal amount of fluid for consumption, and seventy ounces or more may often be taken. Persons of large frame require larger quantities of fluid. Cases of gouty diabetes with corpulency will be benefited by a larger rather than smaller supply of fluid, provided there be no cardiac or renal complications. In albuminuria, which is not infrequently present in obesity, a restriction of fluid is often called for to meet associated cardio-vascular difficulties. If proteids be given in large quantity it is necessary to enjoin abundant water-drinking to carry off the products of nitrogenous metabolism, which would otherwise become noxious. This is an essential feature of the Salisbury plan of treatment. Fats and carbohydrates are elements of food which induce much less metabolism than proteid matters. Proteid food increases both proteid and non-nitrogenous metabolism, and may thus reduce the fat of the body. The gouty habit, with lithæmic tendency, if associated with obesity, demands free dilution. In all these conditions it is proper to take fluids freely about three hours after the larger meals, and not with them. Half a pint of cold or hot water may be also taken early in the morning and late at night. Water taken into an empty stomach is nearly all passed on to the duodenum, but little apparently seems to be absorbed from the gastric surface. To drink freely of water certainly increases metabolism, more urea being discharged than can otherwise be accounted for. If the skin act freely, as often happens in obese persons, more fluid will necessarily be demanded.

Treatment by spa waters.—Certain spas are in repute and much resorted to for treatment of obesity. The springs of Carlsbad and Marienbad are well adapted for many cases. The plethoric form of obesity is that in which most benefit is likely to accrue. Hot alkaline sodium sulphate waters are available at the former, and cold ones at the latter spring. At Carlsbad there are many supplementary measures available for diminishing corpulency: hot mineral, mud, and vapour baths, massage, gymnastics, and electricity are within easy reach of the patient. The functions of the skin, muscles, and gastro-intestinal tract are all stimulated, and active metabolism encouraged.

The Marienbad course is more bracing. The dietary is well arranged, and a general disciplinary regimen is admirably carried out, which is commonly very desirable for obese patients yet difficult to secure to the same extent in other watering-places. This course is not desirable in the case of patients with cardio-vascular derangements, nor in the anæmic class of obese persons. No routine course is, however, pursued, and, under skilled medical supervision, there is no need to fear that any injury may be done by over-treatment.

When a milder course appears desirable, it may be carried out at Homburg, Ems, Kissingen, Tarasp, or Brides-les-Bains. It is often asserted that the special advantages of spa treatment are but temporary. This need not be the case. An obese patient may be set on a right course, but he must continue to pursue it under medical guidance, and carry out the particular diet and habits necessary for his peculiar condition. Relapses are only too common under any method of treatment unless due and permanent precautions are taken. Oertel lays great stress on regulated exercises, such as the gentle climbing, especially in mountain districts, known as the "terrain" cure. He regards spa treatment alone as no specific in these cases, but only adjuvant to other measures, and even harmful when overdone or carried out so as to starve the patient. It is well to repeat visits to such spas as are found suitable whenever possible. In anæmic cases aperient waters containing a little iron are of especial value. Where there is any cardiac weakness or dilatation great care is necessary in enjoining any but very gentle spa treatment, and the fluids should be restricted. The same rule holds good where arterial sclerosis prevails.

If glycosuria is present, Carlsbad treatment, or that pursued at Neuenahr, is advantageous; and the same may be said in respect of the multiform phases manifested by a gouty proclivity.

Roman or Russian vapour baths are available in cases presenting hydræmia, when restriction of fluids is called for. Not more than three baths should be taken in each week while undergoing treatment. Cardiac disturbances may be aggravated by vapour baths.

It is stated by Lahnsen that there is an absolute immunity from obesity on the sea-coasts. This is, perhaps, too general a statement, but there is probably a basis of truth in it, and a seaside residence may be recommended with advantage in some cases of strong predisposition to obesity. Persons of gouty inheritance, many of whom are disposed to undue corpulence, are not, as a rule, well affected by marine influences, and enjoy better health inland, in hilly and breezy countries.

Treatment by thyroid extract.—Some satisfactory results have been obtained of late in the treatment of obesity by the use of thyroid extract. There can be no doubt that this agent has a very marked influence on the nutrition of the skin and integumentary system generally. There is, as yet, however, no certain knowledge as to the particular class of cases in which benefit may be expected. Hence it is not advisable to resort to such treatment indiscriminately. That it is universally applicable can hardly be expected; but it may sometimes prove serviceable in default of other well-recognised methods of treatment, or in addition to them. In any case it must be used with the same strict precautionary measures as are necessary in treating patients for myxœdema.

DYCE DUCKWORTH.

REFERENCES

1. DUCKWORTH, DYCE. "Diabetes in Relation to Arthritism," *St. Barth. Hosp. Rep.* 1882.—2. EBSTEIN, W. *Die Fettleibigkeit und ihre Behandlung.* Wiesbaden, 1882.—3. FOSTER, MICHAEL. *Text-Book of Physiology,* vol. ii. 6th edit. 1895.—4. HARVEY, W. *On Corpulence* (Banting treatment), 1872.—5. LEGENDRE, P. Art "Obesité," *Traité de médecine,* tome i. 1891.—6. MITCHELL, WEIR. *Fat and blood, and how to make them.* 1878.—7. OERTEL. Art. "Obesity," *XXth Century Practice of Medicine,* vol. ii. 1895.—8. PAGET, Sir J. *Clin. Lectures and Essays,* 1879, p. 14.—9. PAVY, W. *Physiology of the Carbohydrates.* 1894.—10. YEO, J. BURNEY. *Food in Health and Disease.* 1889.

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an ordinary epileptic fit. The urine is then found to contain albumin, and he may die comatose, and the kidneys be found in a state of advanced granular degeneration; though no sign of renal disease had as yet attracted attention. Such a man probably belonged to the labouring class, members of which are not keen to take notice of what they consider to be slight ailments.

With the final nervous disturbance there is often delirium, sometimes of a violent character. There is often dyspnœa of the asthmatic type, and sometimes bronchitis. Cheyne-Stokes' breathing is often present, sometimes in a very marked form. With the development of the cerebral symptoms the pulse, probably formerly hard, loses its force, and often becomes extremely feeble before the close. The coma is less profound and less stertorous than that which is produced by cerebral hæmorrhage, and the muscular failure commonly affects both sides alike, so that hemiplegia is absent. The temperature is usually subnormal, though exceptionally, sometimes after a hot-air bath, it has been known to go up even to 103°. It is worth noting that uræmic attacks, whether asthmatic or convulsive, are sometimes determined, in persons sufficiently charged with the poison, by mental emotion.

After death the brain is found to be anæmic, the large vessels empty, the gray matter pale, the white colourless and bloodless. There is generally a slight excess of watery fluid in the cavities and interstices. The ventricles contain a little more than usual, but not enough to cause pressure on the cerebral substance; the sulci are generally deep, and the convolutions prominent. In former times, when uræmic coma was not recognised, this condition was, no doubt, often described as serous apoplexy. The brain is generally firm as in health. I have already referred to an observation of Dr. Carter, to the effect that the brain substance in this condition yields no excess of water.

The urine, with the granular and contracting kidney, differs from that of acute nephritis in certain striking particulars. With the granular or granulating kidney (excepting when this condition is the sequel of acute nephritis) the urinary change is exceedingly gradual and insidious, not only long unnoticeable by the patient, but such as to escape routine medical observation. In the next place, contrary to what happens with acute nephritis, the urine is superabundant at first, scanty at last. Diuresis, a trace of albumin, few casts or none, loss of colour and specific gravity, and the disappearance or diminution of urates, are urinary characteristics of the early stages. Later, particularly when intratubal changes are superadded to the interstitial, the albumin increases, the urine diminishes, and casts multiply. Towards the close the urine often becomes very pale and of very low specific gravity, deficient in acidity, and often of a fishy smell. The urine occasionally contains blood, or gives evidence under the guaiacum test of blood crystalloids. Rarely the secretion is profusely and continuously hæmorrhagic. This, I believe, occurs chiefly when there is much tubal inflammation together with the interstitial—when, in short, the pathological state is mixed. To conclude these general statements, it must be added that all the normal excreta except the water are diminished.

To revert somewhat more in detail to a few of the points which have been touched upon, the quantity of urine, or in other words the secretion of water, is in some cases so excessive as to amount to a sort of diabetes insipidus (90 ounces per diem is not an unknown quantity), with resulting thirst. In the advanced stages the quantity usually falls below normal, possibly to 6 or 7 ounces, or even on the approach of death to total suppression. Diuresis may be looked upon as salutary, and thirst as a natural demand to be satisfied rather than endured. The specific gravity varies inversely with the urine; it may be as low as 1007, or even lower, when the urine is very abundant; if the urine become scanty it may become even higher than normal, 1030 being the maximum of my experience. Next as to albumin, this averages much less than with the kidney of acute or subacute nephritis. The more uncomplicated is the interstitial change the less the albumin; when the kidney, in addition to having a granular surface, is large and congested there may be scanty urine with a large proportion of albumin. The more atrophic the organ the more abundant, as a rule, is the water and the less the albumin. This may be only a trace, and that more apparent with nitric acid in the cold than with heat and acid. It is worth noting in especial that though the cardio-vascular changes may be declared, and the fatal issue not very distant, it is possible that the urine may be absolutely free from albumin. Among the normal solids of the urine the urea, as has been said, is diminished. This diminution affords a rough test of the deterioration of the gland, and of the peril of the patient. The disease may last for a long time with but slight lessening of urea, yet as it progresses the urea diminishes. In a case under my own care the urea gradually fell from 23 grammes to 8·7 grammes in the twenty-four hours; and instances have been recorded by trustworthy observers in which the daily amount has been as low as 3·5 grammes, or even 1·0 gramme. The uric acid follows a similar rule; little reduced at first, latterly extremely so. The mineral acids and the chlorine are lessened, the phosphoric acid more than the sulphuric acid or the chlorine. The alkalies and earths are reduced, but have received less attention than they deserve. The validity of the kidneys should be roughly indicated by the amount of solids passed, exclusively of the albumin, in twenty-four hours. But there are individual differences of food and physiological habit which make it unsafe to draw conclusions except from great or very persistent departures from the normal standard.

The urinary sediment with the granular kidney is less abundant and less constant than with the more acute disorder. Putting aside urates and crystalline deposits as constitutional rather than renal, casts are the chief microscopic products which have to be considered. In quiescent cases these may be entirely absent. The less the tubes are involved the more simply interstitial the disease, the fewer the casts. Their absence is a sign of little morbid activity, their relative abundance a measure of it. Renal diagnosis cannot be founded on casts alone, though they may be helpful to it. The casts which are most frequent with the granular kidney are coarse, dark, and of granular texture. Casts retaining the translucent appearance of fibrin are present as in other forms of renal disease. Epithelial casts are also occasionally found, and must be held to indicate the intercurrence of tubal catarrh. A similar statement may be made with regard to detached renal epithelium. Blood is passed with less frequency than with the more acute disorder. About one patient in ten was found to pass enough blood to be evident to the naked eye.

Treatment.—In the treatment of the granular kidney there is more to be done than might have been expected, considering that the disease is not to be cured, nor has any tendency to recovery. At best it may remain stationary, or advance no more rapidly than age advances to the inevitable and natural end. Our primary guide must be physiological, and our endeavour must be so to modify the circumstances and habits of the patient as to minimise the work of the irritated gland, and enable the system to do with a minimum of renal relief. Diet, warmth, exercise, and elimination by organs other than the kidneys must all be brought under regulation. I will deal first with the quiescent condition and in regard to diet. Nitrogenous food, which supplies the bulk of the renal excreta, should be reduced to the lowest amount compatible with health, having regard to the fact that though uræmia threatens on one side, anæmia is to be feared on the other. The rule I have found beneficial is one meal of flesh, one of fish, and one of neither. Every kind of vegetable food may be allowed, more particularly the farinaceous: the

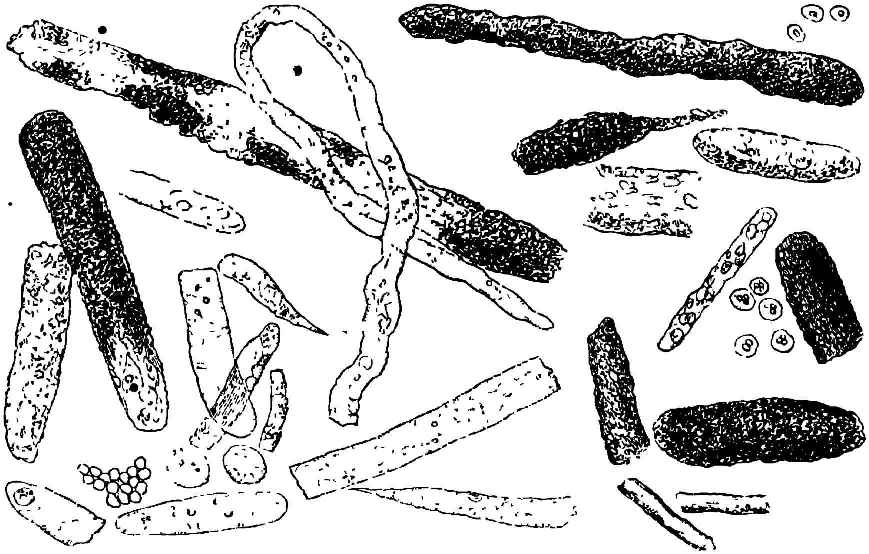

FIG 4.—Casts obtained from cases of granular kidney. Most contain coarse dark granular matter, others granular matter of finer texture, a few contain blood-globules or epithelial cells. (From Dickinson's *Albuminuria*.)

patient may eat potatoes with the Irishman, oatmeal with the Scot, rice with the Hindoo, or pulse with the Prophet. Regard must of course be had to individual taste and suitability. As to liquids, the liberal use of water or aqueous drinks should be enjoined. Milk may be employed freely, though I have not found quiescent cases to do well on a purely milk diet. Alcohol should be avoided, or used with extreme parsimony. Next, as to the temperature to which the body should be exposed. As long ago as 1867 I advocated resort to a warm climate as a remedy in chronic albuminuria. Cold to the surface is a renal stimulant, and warmth a condition in which the kidneys are comparatively at rest. In subtropical regions albuminuria, excepting perhaps that which depends on lardaceous disease, is infrequent as compared with what occurs in the colder parts of the temperate zone. Thus England is more albuminuric than the south of Europe or the north of Africa. The desiderata are warmth, dryness of air, and equability; of these equability is of less importance than warmth and dryness, as the valetudinarian may keep within doors after sunset. To speak meteorologically, what should be sought is a high mean temperature within temperate limits, a low relative humidity, and a small daily range. I have elsewhere discussed renal resorts in more detail than is possible here; to condense the conclusions they are these: If the health and means of the patient are such as to allow him to make a long journey, let him go to the north of Africa, Egypt, or Algiers. The Riviera is disappointing, occasionally cold during the day, and always so after sunset; the latter disadvantage is, however, shared, and even to a greater degree, by many other subtropical places. If the patient cannot go farther than the Riviera, I think he may as well stay within the circumference of Great Britain, within which, on the whole, I think the best winter resort is Falmouth. The daily range is here very slight, the nights only about seven degrees colder than the days, while the humidity, though considerable, is less than at Penzance, a town which will necessarily be taken into comparison. To minimise the cold of the winter without leaving England it is necessary to go to the west, so as to be within the influence of the Gulf Stream, and to the south where high land interposes between the selected spot and the north wind. It should be endeavoured, also, to obtain similar protection from the east—often a matter of some difficulty. Other matters beside climate which concern the warmth of the body must not be lost sight of, notably the employment of warm clothing and the avoidance of cold bathing. Habitual exposure to cold may result in the chronic aggravation of the disease. Incidental exposure may give cold to the kidneys, or, in technical language, set up intercurrent nephritis—an accident especially to be guarded against. Touching intercurrent nephritis I may recall what I have already said, that there is reason to believe that foul smells are capable of giving rise to it. Exercise must find brief mention. Walking is the best. Cycling, I think, is less suitable, at least I have known a temporary attack of albuminuria of the nature of nephritis to follow a day's bicycling.

The use of drugs when the disorder is quiescent takes a secondary place. It is well to give none unless there be some especial indication. It is essential, however, by their means or otherwise to secure regular and somewhat full action of the bowels, which should be moved freely once a day, or perhaps three times in two days. An occasional morning potion of sulphate of magnesia, or one of the effervescing salines which contain it together with an alkali, answers well. This may be varied with a nocturnal dose of compound rhubarb, colocynth, or cascara. If the urine be over-acid a little tartrate of potash or potassio-tartrate of soda may be given twice a day. Iron has its use and also its abuse. It should not be given as a matter of routine, but when an obvious condition of anæmia suggests it. When given it should be, as a rule, associated with enough of some aperient to rather more than overcome the constipating action. Ten drops of the tincture of the perchloride, with a little sulphate of magnesia, of soda, or of potash, to which may be added ten or fifteen minims of aloes wine, will generally serve the purpose. Sulphate of potash is useful in this relation, because a little of it suffices. Ten grains are generally enough together with the aloes. If it is desired to produce an alkalising effect, two or three grains of ferrum tartaratum may be put with a little tartrate of potash or the potassio-tartrate of soda, and perhaps a drachm of the compound decoction of aloes. I have found it expedient to give such a mixture as I have indicated at bed-time and on rising. The nocturnal dose insidiously prepares for what the morning dose completes.

Should dropsy appear, it must be treated as recommended in nephritis. For œdema the horizontal posture when at rest; though moderate walking may often be permitted with advantage. Digitalis, intermitted from time to time, need not again be insisted on as a prime necessity in renal dropsy. A drachm, or less, of the infusion, or ten drops of the tincture, may be given with a little perchloride of iron and one of the sulphates. Acupuncture can generally be avoided. In the advanced stages of the disease, if dropsy of the cavities present itself, tapping either of the pleuræ or the peritoneum may be employed with little danger and much advantage. Should pulmonary apoplexy or hæmoptysis occur, it should not be treated with ergot or styptics, but with laxative salines, especially sulphate of magnesia. Having regard to the hardness of the pulse, should this be excessive it may be modified by moderate purging, but under no circumstances should the attempt be made to reduce the pulse to the softness of health. The circulation is carried on under difficulties, and more than normal pressure is essential. If any of the lesser manifestations or threatenings of uræmia present themselves, headache, vomiting, uræmic smell, or extreme poverty of urine without any commensurate increase of quantity, much may be done by periodic sweating. The best way of accomplishing this is by Turkish baths, one every ten days or fortnight. But these are not always available. The best substitute is the leg-bath of which I have already spoken, which may be applied weekly or at intervals of ten days. The medicinal diaphoretics, excepting sometimes pilocarpin, are of no great use; the acetate of ammonia is possibly injurious, as tending to increase the ammonia in the system, which, if we may judge by the breath, is already too abundant.

The therapeutics of renal asthma must be directed to two ends the immediate relief of the spasm and the mitigation of the uræmia with as little delay as is practicable. The spasm may be notably reduced by vaso-dilators and etherial and alcoholic stimulants. The inhalation of nitrate of amyl is of the greatest use; I have had less experience of nitro-glycerine, but cannot doubt that this also is useful. I have used also opium and stramonium, but am satisfied that these are less beneficial than vaso-dilators and etherial stimulants. But measures which purify the blood and at the same time reduce the arterial tension are of more permanent effect than antispasmodics. Purging and sweating, calomel, elaterium, hot-air baths, and pilocarpin are the agents and the instruments from which the most lasting good may be expected. By such antiuræmic treatment the attacks can often be held at bay with long intervals of peace until the patient finds leisure to die quietly in some other way.

The uræmic convulsions, which are too often fatal, though not necessarily so, and the uræmic coma of quiet onset which is generally fatal, must be met energetically in modes which have been referred to in connection with nephritis. Prompt purging and sweating must be had recourse to, and possibly, if the pulse be extravagantly hard, venesection may be indicated. If the convulsions are very violent there is no objection to the inhalation of chloroform, or the use of chloral by the mouth or the rectum. Of late the inhalation of oxygen has been recommended. Theoretically this seems worth trying. I have had little experience of it in uræmia, though I have frequently employed it in diabetic coma, but without benefit. Finally, opium and its derivatives should be rigidly avoided in the convulsive and every other stage of organic albuminuria, save only with the lardaceous kidney, where they are permissible and sometimes useful, but not when this condition is productive of convulsion or any other uræmic symptom.

III. LARDACEOUS DISEASE OF THE KIDNEY.—Lardaceous renal disease has already been so far discussed in relation to lardaceous disease in general (vol. iii. p. 259), that it is not necessary to say anything with reference to pathology or etiology beyond what has already found mention. It only remains to add a few clinical details bearing upon symptoms and treatment.

Nothing further need be said as to the sex and age of the subjects of the disorder in question. It is not necessary to repeat that lardaceous disease, whether of the kidney or of other organs, is always secondary, always gradual in commencement, and always chronic in progress; though it may undergo the superaddition of tubal or diffuse nephritis which may convey to it originally for the time as much acuteness as belongs to renal inflammation of other origin.

The detection of the disease is generally easy, even obvious, though occasionally a searching inquiry has to be made before its nature is apparent. The question will probably be raised by the discovery of albumin in the urine, or the presence of œdema or diarrhœa. What we then have to search for is evidence of suppuration or of syphilis. The suppuration may be present or past; if any chronic suppurative disorder still persist, it will at once convey a suggestion, as also will any deformity, deficiency, or cicatrisation which a bygone suppurative process has left as its record. Signs of phthisis, a crooked spine, a defective joint, an absent limb, or extensive scars may all be instructive in this relation. A tropical complexion may give a hint; the disease is readily produced under the influences of the tropics, the traveller is likely to have had dysentery in these regions, and he may even have had, and survived, abscess of the liver. Signs of syphilis will be equally indicative, eruptions, nodes, and evidences of old specific ulceration. It is obvious that there must be some cases, however few, in which the agencies in question may have done their work and left no mark. Suppuration may take place from the bowel as the result of dysentery or some other ulceration, and leave no external sign; the same may be said of the kidneys, one of which may be destroyed by a suppurative process which may have come to an end before the constitutional result is recognised, so that then there is no ostensible evidence of the primary mischief. Syphilis also may leave its effects on the constitution in the form of lardaceous disease without any conspicuous external mark. However, I need not here dwell on the causes of lardaceous disease, which have been already given in detail; my present object is only to point to the external signs which may lead to its detection. A worn and cachectic look is very significant, though it may not at once be apparent on what it depends.

Putting aside evidences of antecedent disease the lardaceous state is early productive of an increase in the quantity of urine, which is slightly albuminous. The increase may amount to morbid diuresis, and be attended with thirst. Diarrhœa is a frequent symptom, important not only diagnostically, but as a source of danger which contributes largely to the fatal issue. This is generally painless, the motions watery and free from mucus. It is due to extension of the disease to the intestine. Vomiting due to a similar participation on the part of the stomach is often distressing and sometimes dangerous. The enlargement of the liver and spleen has been sufficiently referred to in the general account of the disease. These enlargements, when present and palpable, are great helps to diagnosis, but are less productive of symptoms than might have been expected. The enlarged liver is seldom attended with obstructive results, and the enlarged spleen does not usually give rise to marked leucocytosis. Dropsy is present at some time or other, more often than not. I reckon that œdema occurs in about two-thirds of the cases, ascites in about a fourth; hydrothorax rarely; dropsy of every kind may be absent from first to last; diuresis and diarrhœa are antagonistic to it. Though there may have been considerable swelling in the course of the case, diarrhœa towards the close may completely carry it off, and leave the patient attenuated and sharp-featured, with dropsy, so to speak, a minus quantity. Œdema is most apt to come on when, with the advance of the disease, the profuse and slightly albuminous urine has become scanty and highly albuminous. I have often noticed the œdema to present more the characters of heart disease than of renal; absent from the face, and collected in a peculiar baggy manner about the ankles.

As with other renal maladies there is a tendency with lardaceous disease to certain intercurrent affections. Pneumonia, pleurisy, pericarditis, and peritonitis occur in this relation, but less frequently than with nephritis or the granular kidney. These inflammations are probably due to a uræmic state of the blood, a condition which is less apt to be developed in lardaceous than with other renal disorders. They are more frequent when the lardaceous state is chiefly renal than when the stress falls mainly on other organs. In forty-eight cases of lardaceous disease, in which the renal change was productive of marked symptoms, pneumonia was found in nine, pleurisy in five, peritonitis in four, and pericarditis in three. Bronchitis is seldom present. Hæmorrhagic complications are rare. Of these, epistaxis is the most frequent. Purpura is uncommon, but not unknown. Sanguineous apoplexy and the albuminuric retinal affection present themselves but rarely in connection with lardaceous disease, and then only in cases of long standing where the fibrotic change has been superadded. Apoplexy has been recorded in this relation, though this event does not chance to have come within my experience. I have known a case, however, in which well-marked retinal hæmorrhage occurred in connection with advanced renal disease of the kind in question. As to albuminuric ulceration of the bowel, I knew, and have elsewhere related, an instance in which this affection and lardaceous disease were conjoined; but in this case the ulceration, and an abscess to which it gave rise, were the causes of the lardaceous disease, not its consequences.

The absence of hæmorrhagic results is explained by the general absence in lardaceous disease of increase of arterial tension and cardio-vascular hypertrophy. The heart in this disorder gives an average weight of 10⅔ ounces for adult males, one of 8½ ounces for adult females, which are so nearly the weights in health that it is clear that hypertrophy is generally absent. The left ventricle is somewhat thinner than in health, and the cavity of full size or somewhat dilated. The heart is weakened rather than strengthened, and the œdema, since it affects the ankles rather than the face, is suggestive rather of a cardiac than a renal origin. It must be added that in certain cases, as has been already noticed, the fibrotic renal change may be superimposed upon the lardaceous with some degree of the cardio-vascular thickening which belongs to renal fibrosis. I could instance a man who died of lardaceous disease consequent on dysentery. He eventually had uræmic symptoms. The heart was distinctly but not greatly hypertrophied, weighing 13 oz. The general absence of cardio-vascular hypertrophy in the lardaceous state may be associated with the condition of arterial tension, which is usually diminished rather than increased. This may be traced to two causes: there is often some exhausting discharge, suppurative or diarrhœal, which keeps the tension down; the tendency to uræmia is

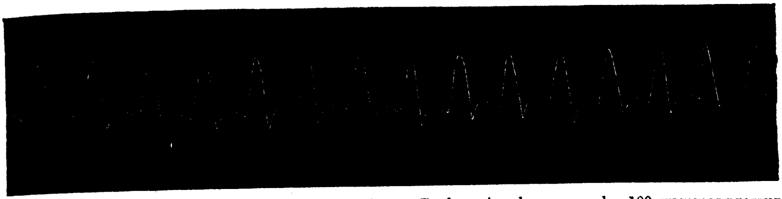

FIG. 5.—Pulse-tracing in lardaceous disease of kidney. Dudgeon's sphygmograph. 100 grammes pressure.

comparatively slight, so that the vascular obstruction due to this morbid state of blood is absent. In connection with the general freedom from over-tension in the circulating system may be mentioned the infrequency of renal asthma with lardaceous disease.

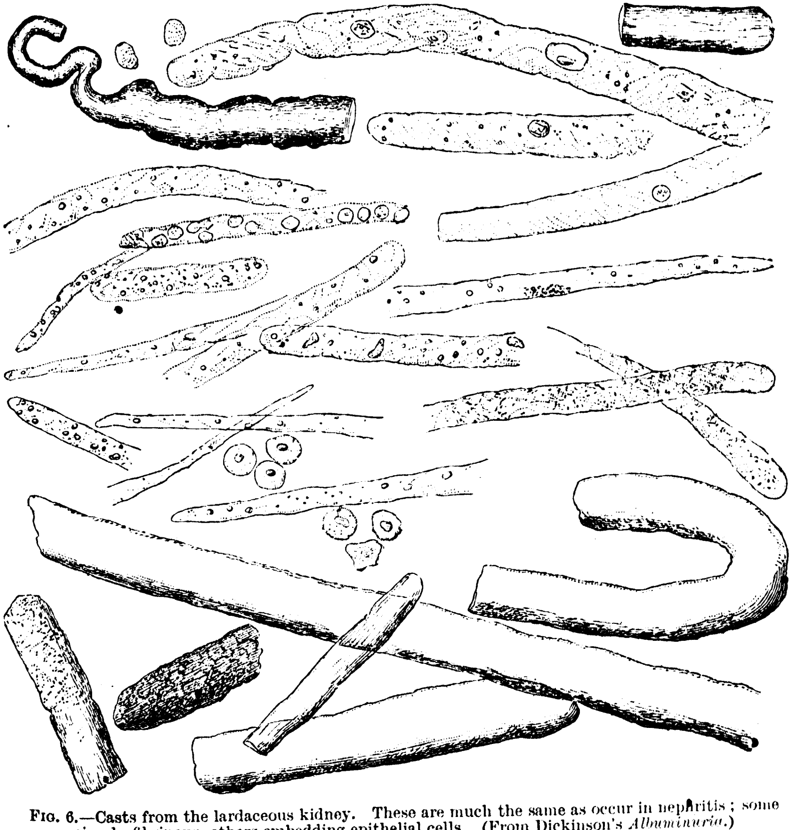

FIG. 6.—Casts from the lardaceous kidney. These are much the same as occur in nephritis; some simply fibrinous, others embedding epithelial cells. (From Dickinson's *Albuminuria*.)

While upon the heart in lardaceous renal disease, I may add that endocarditis is relatively frequent. Vegetations recent at death were found in five of eighty-three cases, and old valvular thickening in twenty-one of the same series. The vegetations are often ragged, and have been known to present the special reaction with iodine, as also have embolic blocks to which they have given rise. This tendency to fibrinous deposition on the valves must probably be attributed rather to the state of the blood in the general lardaceous condition than to any action belonging especially to the renal localisation.

Not only does renal fibrosis ensue upon the lardaceous state, which may be said to be the rule when the disease is of long continuance, but it sometimes comes to pass that acute nephritis with much tubal catarrh is superimposed upon it. In such a case there may be an exacerbation of dropsy, with scanty and highly albuminous urine, abundance of epithelial and other casts, and a copious deposit of renal epithelium.

The duration of lardaceous disease is exceedingly variable, sometimes it approaches in rapidity all but the most acute forms of tubal or diffuse nephritis, sometimes it imitates the slow progress of the most chronic forms of the granular kidney. From the necessarily gradual operation of the causes on which it depends, it is obviously difficult to mark the beginning with exactness. The cause in every case must have been in existence for some time before the effect was produced. I have before me a collection of post-mortem cases representing the experience of St. George's Hospital from the year 1876 to 1894, of which an abstract is appended. It must be borne in mind that as the recognition of the lardaceous state was post-mortem, not clinical, there were many in which it had not progressed far enough to cause symptoms.

TABLE of 78 Cases in which Lardaceous Disease was found after Death, showing the Time between the Commencement of the Disease by which it was caused and the fatal Termination.

Time.	Number of Deaths in stated time.		
	Kidneys affected.	Kidneys not affected.	Total.
From 2 to 3 months	1	1	2
Over 3 months not above 6	5	...	5
,, 6 ,, ,, 12	20	4	24
,, 1 year ,, 2	16	...	16
,, 2 years ,, 5	8	2	10
,, 5 ,, ,, 10	9	3	12
,, 10 ,, ,, 20	5	...	5
,, 20 ,, ,, 30	1[1]	1	2
,, 30 ,, ,, 32	2		2

It is apparent that in the majority of cases the fatal termination was within two years of the origin of the disease. In some the disorder appeared to have originated only two, three, or four months before death. The shortest time, two months, was presented by a single instance in which the cause was phthisis; the overt manifestations of this disease, from which the history was dated, may have been preceded by changes which were unnoticed or unrecorded. To pass to the other end of the scale there were some cases where the presumed source of the morbid condition dated as far back as twenty or thirty years. One patient in whom the disease was presumably due to congenital syphilis lived to the age of twenty-one. The longest interval between the beginning and the end was exemplified by a man who died at the age of fifty-seven, with cerebral syphilis and many manifestations of lardaceous disease, in whom the specific history was traced back for thirty-two years. It was not known when he began to be lardaceous.

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[1] This case was apparently due to congenital syphilis.

In the earlier and possibly in the longer part of its course lardaceous disease may be latent or without symptoms. When these present themselves it may be presumed that the organic change has already made considerable progress. How long it may last after it has been declared by albuminuria, diuresis, thirst, or dropsy is a matter of much variation, but it may be said, as relating to the majority of cases, that the end of the complicated process is not far off, the interval to be measured by months more often than by years. In some cases, however, the larger measure of time is required to express the duration of the symptoms. A boy, a frequenter of the Hospital for Sick Children, had a profuse discharge in connection with disease of the pelvis and hip-joint, and a year afterwards displayed evidences of lardaceous disease in enlargement of the liver and spleen, slightly albuminous urine, and some œdema. Under the influence of tonics and Margate the liver gradually resumed its normal size, the urine ceased to be albuminous, and he lost the œdema. The spleen remained greatly enlarged, but he improved so greatly in general health that his complete recovery seemed not improbable. He was, however, attacked with hæmoptysis, with a return of the dropsy, and died eight years after the commencement of the lardaceous symptoms.

A man, in whom the disease was of syphilitic origin, became my patient in October 1866 with hepatic enlargement, albuminous urine, and œdema. He improved under specific treatment, and lived until June 1869.

A boy, in whom the disorder was due to disease of the pelvis, lived for nineteen months after the legs had become œdematous, the liver having enlarged previously. These instances of protraction might be multiplied and extended, but, nevertheless, it may be fairly stated that commonly the duration of the symptoms ranges from about two months to a year and a half. It will be evident to the reader that the foregoing statements are based entirely on fatal cases, in which the evidence may be taken as complete and conclusive; but it is not to be inferred from the exclusion of others that all cases are fatal.

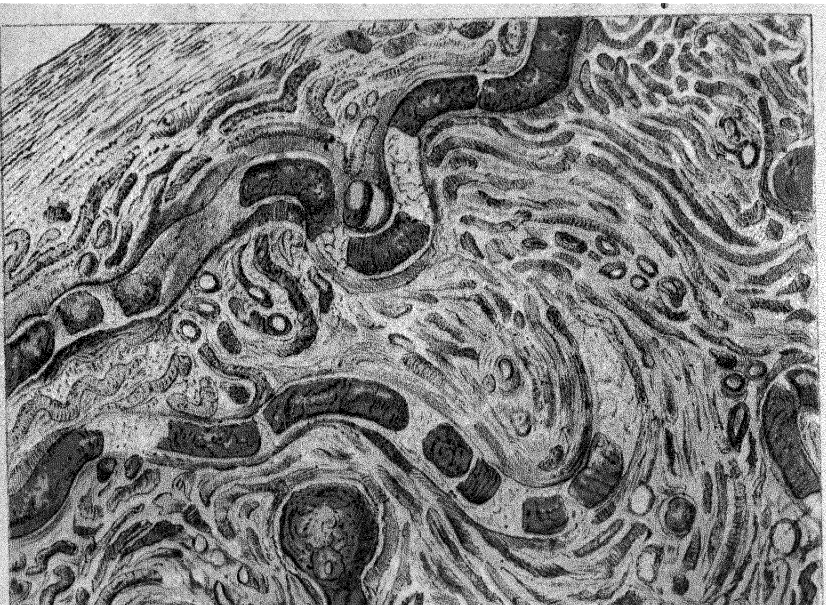
The immediate causes of death under lardaceous disease in general have already been stated in detail (vol. iii. pp. 274, 275); it only remains to add a few words in reference to the renal localisation. Of persons shown after death to have been the subjects of lardaceous change, a greater number, as has already been shown, owe their deaths directly to the primary lesion rather than to the lardaceous consequence. Having regard only to the lardaceous consequence, the chief difference between this and other renal diseases is in the relative infrequency in this of uræmia, and the almost total absence of the disorders of over-tension, especially of hæmorrhage, cerebral, retinal, and of the nature of pulmonary apoplexy. The annexed statement, derived partly from my own experience and partly from the St. George's records, will furnish sufficient evidence on the points in question. It is here seen that the chief cause of death in lardaceous disease is diarrhœa; this is not strictly renal, but due to the participation of the bowels in the disease. Diarrhœa was prominent as a cause of death in 29 of the 74 cases, about a third. Vomiting was prominent as a cause of death in 9.

Inflammatory affections of the lung are of frequent occurrence, as with other forms of renal disease. Cerebral uræmia occurred in 13 of the number, about 1 in 6, a small proportion compared to what holds in other forms of renal disease. The attacks take place sometimes with convulsion, sometimes as coma without convulsion. It is not necessary to add anything to what has been said with regard to uræmia under other circumstances. The condition of the kidneys is not such as to offer much hope in treatment, beside which the state of the patient is usually such as to forbid very energetic or exhausting measures.

TABLE showing the apparent Causes of Death in 74 cases of Lardaceous Disease, in which the Kidneys were affected. No symptoms are given excepting such as were mainly concerned in the fatal issue:—

Diarrhœa	23
Diarrhœa + vomiting	4
Diarrhœa + dropsy	1
Diarrhœa + erysipelas	1
Vomiting	3
Uræmia (convulsions or coma)	13
Pneumonia	9
Broncho-pneumonia or bronchitis	2
Pleurisy	2
General dropsy	3
Ascites (tapping)	4
Peritonitis	5
Enteritis	1
Thrombosis	2
Suppression of urine	1
	74

I have already pointed out the fact (see vol. iii. p. 276) that lardaceous disease has to a certain degree a tendency to recovery; this will be further seen when I come to consider the results of treatment.



Section of a lardaceous kidney showing casts *in situ*, presenting the iodine reaction, which casts rarely show. (From Dickinson's *Albuminuria.*)

I have it on the authority of the late Dr. Moxon that lardaceous organs may recover themselves under the influence of typhoid fever, as if the material were consumed by the febrile process.

The urine in lardaceous disease of the kidney resembles in many particulars that of granular degeneration. The first change is increase of quantity, which varies from little above the normal to about four times as much. Sir. T. Grainger Stewart has found as much as 200 ounces in twenty-four hours. The common range is from 50 to 90 ounces. The urine thus increased is pale and clear and of low specific gravity, from about 1015 to 1006. When the increase becomes obvious, or soon afterwards, a trace of albumin appears. Commencing always in small quantity, it gradually increases to a decided precipitate while the quantity of urine diminishes. Towards the latter periods, particularly when a certain amount of tubal catarrh is superadded, the urine may fall below normal even to 8 or 10 ounces in twenty-four hours, and will now be highly albuminous. On the approach of death the secretion may be totally suppressed, though this is exceptional. The acidity of the urine is usually decreased. Blood is but rarely present; when present it is sometimes in considerable quantity. Casts make their appearance early and increase in number as the disease progresses. The most common are cylinders of fibrine, often dotted with oil, which do not differ from what are shed in other renal disorders. They may be large or small according to the state of the tubes in respect of dilatation and the retention of their epithelial lining. Besides these there are often others which contain or chiefly consist of epithelial cells; these indicate tubal catarrh, and may be associated with much loose renal epithelium. As a very exceptional occurrence, but as one which admits of no doubt, it must be mentioned that casts have been known to present the iodine reaction in a marked manner. I have witnessed this both in casts which have been passed with the urine, and also in those which have been exposed *in situ* in the kidney by section after death. I have given a coloured illustration of this phenomenon in the second edition of my book on *Albuminuria*.

It is by no means rare when the urine is scanty to find a deposit of uric acid or amorphous urates.

The chemical changes in the urine may be briefly expressed. All normal ingredients are reduced excepting the water, about which no more need be said. The urea is but slightly reduced so long as the urine is superabundant; afterwards it is more sparingly secreted, but seldom reaches the degree of diminution to which it falls in extreme cases of other forms of renal disease. The ordinary range is from two-thirds to half the normal quantity; 7·37 grammes and 3·6 grammes have been recorded—the first by myself, the second by Rosenstein—as examples of unusual diminution. The uric acid is sometimes normal in quantity, more often diminished. The phosphoric acid, the sulphuric acid, and the chlorine are all lessened, the phosphoric acid with the greatest regularity. The alkaline salts, as estimated by incineration, are below the normal amount; especially during the presence of a purulent discharge. Nothing need be said about the albumin but what has already found place. It may be observed that in lardaceous disease the precipitate is sometimes more soluble in excess of nitric acid than is usual with other forms of renal disease.

In the *treatment* of lardaceous disease it has to be premised that the disorder, as already stated, has a tendency to recovery which, however, is to be little relied upon when the disorder is advanced, and of the kidney. The superaddition of fibrosis stamps the disease with permanency, though the lardaceous character may be on the wane or even a thing of the past. If the cause is apparent, but the effect not yet manifest, prevention must be aimed at by removal of the cause. If the change be noticeable, but as yet only incipient, its further progress may be arrested, and even the mischief undone, by directing salutary influence upon the primary disease. The paramount measures are the arrest of suppuration and the counteraction of syphilis. Of late years we have seen much less of lardaceous disease than formerly; this is owing, in the first place—speaking in order of time—to our having learned the use of iodide of potassium; and in the second place, to the introduction of antiseptic surgery, which has made operations possible which formerly were not so, and has prohibited suppuration under circumstances in which it used to be uncontrolled.

The first question in the treatment of lardaceous disease is to which of its two causes it is due. Supposing it to be due to present suppuration, we must take counsel with a surgeon, and put an immediate stop, if it be possible, to the source of the discharge and of the disease. The expedients of surgery must be pushed to the uttermost in the assurance that if the primary mischief be allowed to continue, the secondary mischief will probably kill if the primary do not. On the other hand, we have warrant for believing that if the organic change be not far advanced, it may be undone by the processes of nature if the cause be removed. The subjects of lardaceous disease have a considerable power of recovery after operations, and will bear much in the way of what is necessary to arrest suppurative processes. Together with appropriate surgery, or without it when this is not practicable, much may be done by general restoratives. If we cannot stop the discharge, we may compensate for it. Nourishing food, cod-liver oil, iron, and quinine are all of value towards this end.

In the presence of suppuration I am sure it is harmless, and I think it is beneficial, to compensate the inevitable loss of potash by the administration of this alkali. This to be effective must be in its most active form, that of liquor potassæ, and be given on an empty stomach. The amount thus introduced is small, but it carries with it active affinities. Some of the old belief in liquor potassæ as a resolvent may be due to its action under such circumstances as I have indicated. Pure and bracing air is of particular efficacy.

Margate has obtained great and deserved repute in cases of suppurative disease; it seems both to control the suppuration and to mitigate its effects. I have known lardaceous cases with present suppuration, which had been practically but not wholly checked by operation, to derive undoubted benefit from the local influences, and I have referred to one in a former page (vol. iii. p. 276). Other places beside Margate may have similar effects, but of all such Margate may be taken as the example.

In treating established lardaceous disease it may be a matter of rejoicing to the physician to be able to trace it to syphilis. The great remedy is iodide of potassium in large doses and for a long time; the results, though slowly brought about, are eminently satisfactory. Such patients do not bear mercury well, and my experience has led me to avoid it. I have elsewhere given instances of the effects of iodide of potassium in these circumstances which I need not here repeat. It will suffice to say, under the persevering use of this remedy, that I have known marked lardaceous disease of syphilitic origin, with highly albuminous urine and much dropsy, to eventuate in recovery apparently complete. Given for a short time it is useless, and the good effects I have seen have been from large doses. It needs to be given with occasional intermissions for from two to five years, and perhaps in doses of from ten to twenty grains three times a day. Iodide of iron can often be usefully associated with it. Such treatment will be more than equally serviceable in relation to lardaceous viscera other than the kidneys when of syphilitic origin. I have known the enlarged liver to lessen rapidly, and ascitic fluid to become quickly absorbed. The spleen loses its abnormal bulk more slowly than the liver. Of all lardaceous organs the kidney is the most obstinate. There are few diseases which are attended with as much organic change as the lardaceous effect of syphilis and which are impressed by treatment so satisfactorily.

It remains only to add a word or two as to what should be done for some lardaceous symptoms which have not been dealt with in this view. It is not necessary to repeat much that has been said with regard to other forms of renal disease which may be applied with modification to this. It is to be borne in mind that arterial tension is more often below than above par, and that the treatment in general must be less exhausting and more sustaining than with other renal disorders. There is less tendency to uræmia, and less need for stimulating the secretions which is often overdone by the disease itself. For dropsy iron is generally required, and digitalis often beneficial. Intercurrent inflammations should be treated on general principles, but with a light hand. Diarrhœa, as one of the most fatal of lardaceous affections, is one over which medicine has little control. Ferruginous styptics may be employed, one of the best being iron-alum. Vegetable astringents may be used, including the red gum of Australia. And it is to be particularly noted that opium and its derivatives are not counter-indicated, or not to the same extent, as in other varieties of albuminuria. Opium, in the guise of compound kino powder, or with sulphuric acid or sulphate of copper, may be employed. It is well, perhaps, to avoid acetate of lead in such circumstances, as lead is a renal irritant, and lardaceous kidneys especially amenable to irritation.

W. Howship Dickinson.

REFERENCES

1. ALLBUTT, T. C. "Mental Anxiety as a Cause of Granular Kidney," *Brit. Med. Jour.* Feb. 10, 1877.—2. Baillie Lecture, *Lancet*, July 20, 1895. Reprinted in *Occasional Papers on Medical Subjects*, 1896.—3. BRIGHT. *The Reports of Medical Cases*, vol. i. plate 5.—4. CARTER, W. Bradshaw Lecture, *Lancet*, 25th August 1888.—5. DICKINSON. *Albuminuria*, 2nd ed. p. 79, illustrations, pp. 30, 169, 310.—6. *Idem. Medico-Chirurgical Transactions*, vol. xliii.—7. *Idem.* "On the Morbid Effects of Alcohol," *Med.-Chir. Trans.* 1872, vol. lvi. Republished in *Occasional Papers on Medical Subjects*, 1896, p. 65.—8. *Idem.* "The Cardio-Vascular Changes of Renal Disease," *Lancet*, 20th July 1895. Reprinted in *Occasional Papers*, p. 190.—9. *Idem.* "On Albuminuric Ulcerations of the Bowels," *Med.-Chir. Trans.* vol. lxxvii. Reprinted in *Occasional Papers*, p. 161.—10. *Idem.* Croonian Lectures, *British Medical Journal*, April 22, 1876; *Med.-Chir. Trans.* 1891, vol. lxxvii. Reprinted in *Occasional Papers*, 1896.—11. *Idem.* "Case of Uric Acid obtained from the Brain in a Case of Renal Disease," *Path. Trans* vol. xviii. p. 19.—12. *Idem.* "Places and Commonplaces in Renal Disease," *Lancet*, 10th February 1894. Reprinted in *Occasional Papers*, p. 178.—13. *Idem.* "Renal Dropsy," *Med.-Chir. Trans.* vol. lxxv. p. 365.—14. KLEIN. *Path. Trans.* vol. xxviii p. 430.—15. LANCASTER, LE CRONIER. "On Eight Cases of Uræmic Eruptions of the Skin," *Transactions of the Clinical Society*, vol. xxv. p. 49.—16. DICKINSON, W. H. *Pathological Transactions*, vol. xl. p. 145.—17. *Ibid.* vol. xxx. pp. 543, 545.—18 *Medico-Chirurgical Transactions*, vol. xliii.—19. SMITH, PYE. "Affections of the Skin occurring in the Course of Bright's Disease," *British Journal of Dermatology*, vol. vii. p. 284, 1865.—20. TRIPE. *See* Dickinson's *Albuminuria*, 2nd edit. p. 35.

W. H. D.

OTHER DISEASES OF THE KIDNEY

PERINEPHRIC EXTRAVASATIONS

Air.—Air is occasionally found in considerable quantity around the kidney after injury to this organ. The source of the air is not always traceable. In one case it appeared to have gained admission through a perineal incision which had been made on account of a rupture of the urethra, which complicated a fracture of the pelvis. Wounds of the loin, groin, and perineum, whether complicated by wounds of the bowel or not, and fractures of the lower ribs, with injury to the lung, may be the causes of this form of extravasation. Retroperitoneal abscess opening into the bowel may give rise to it.

Blood may be effused around the kidney from a ruptured artery or vein, or from capillaries as a result of violence. The clots so formed may ultimately break down and lead to suppuration. Fractures of the pelvis or lumbar vertebræ, ruptures of muscles, and the bursting of an aneurysm of the abdominal aorta, have been causes of considerable circumrenal hæmorrhage. The kidney may be pushed forward so completely by the extravasated blood as to present a tumour anteriorly in the hypochondrium.

The *symptoms* vary with the cause and extent of the extravasation. When the blood is confined to the cellular tissue of one loin, it causes a tumour, sometimes difficult to diagnose from a distended kidney. If the source of the bleeding be a superficial laceration of the kidney, or a rupture of an artery (say one of the lumbar arteries), some weeks may elapse before the effusion is sufficient to give rise to any swelling or increased dulness in the loin, and no sign of faintness is noticed at any time; then, after some time longer, the effused blood becomes more solid, and the tumour more irregular, and by degrees, perhaps, it is absorbed. On the other hand, the blood-clot may disintegrate; under which circumstances the symptoms of suppuration will arise.

Recovery may take place after very extensive traumatic hæmorrhage; but retroperitoneal hæmorrhages due to ruptured aneurysm are almost certainly fatal, though, it may be, tardily so.

If the hæmorrhage increase, or suppuration occur, and surgical aid is not brought to bear upon the case, death may follow from peritonitis, due to tension upon the peritoneum or rupture of it; or the colon may be penetrated and fæces and flatus enter the blood tumour, and give rise to decomposition, septic absorption, and death.

When hæmorrhage is due to aneurysm, little or nothing in the way of treatment will avail; when due to injury, the treatment must be based upon the principles stated in dealing with injuries to the kidney.

Urine is extravasated into the loin behind the peritoneum from a rupture of the kidney involving the calyces or renal pelvis, from direct penetrating wound, the result of operation or accident, or as a consequence of ulceration of these parts. Ulceration of the ureter, due to injury or the pressure of a tumour, may cause urinary extravasation into the loin or iliac region. The inflammation of the cellular tissue, resulting from urinary infiltration, may run on to suppuration, giving rise to a lumbar or inguinal abscess. Healthy urine alone is but little irritating; it is the mixture of blood and urine which tends to decomposition and suppuration. If the quantity of urine effused is small, the cellulitis, stopping short of suppuration, may become chronic, spreading towards the iliac fossa, and causing contraction of the ilio-psoas muscle. In some instances the effused urine becomes encapsuled within a thick-walled cyst of inflammatory origin, with the cavity of which the kidney communicates at the point of rupture or ulceration. Sometimes phosphates accumulate in the space occupied by the effused fluid to such an extent as to form deposits which block the drainage-tubes used in treatment by lumbar incision.

Treatment.—When the diagnosis is uncertain, but from the fulness and dulness of the loin there is reason to think urine is escaping behind the peritoneum, a lumbar incision and drainage are needed. Suppuration must be dealt with by early free incision. If the kidney be greatly damaged, nephrectomy will be requisite.

RENAL FISTULÆ

Fistulæ which communicate with the kidney and pelvis of the kidney.

Causes.—Renal fistulæ are caused, in the great majority of cases, by calculi in the pelvis of the kidney or in the ureter. Other causes are gun-shot, punctured or incised wounds, injuries inflicted by surgical operation, and abscess of the kidney. The opening into the cavity of the kidney or ureter is usually single and connected with the posterior aspect of the organ. Renal fistula may open at the loin or groin, into the colon or duodenum, into the pleural cavity or lung, or into the peritoneum. It is comparatively rare for a fistula to open into the peritoneum. If the fistula be the result of a wound or a ruptured hydronephrotic cyst, *urine*, sometimes in large quantity, will escape from it; if the effect of pyonephrosis, due to ureteral obstruction, *pus* will be mingled with the urine; if caused by the conversion of the kidney into a scrofulous abscess cavity the discharge will consist of pus and broken-down tuberculous material.

Renal fistula opening in the loin.—When fluid of a urinous character escapes from a fistula which followed suppurative nephritis or injury to the kidney, the diagnosis of the renal origin of the fistula is certain. It must be remembered, however, that a lumbar fistula, instead of communicating with the kidney at all, may be the result of disease in the ureter, the bladder, or even the urethra.

Treatment.—The skin around the orifice must be kept clean, and free from irritation. If, after a fair length of time has been allowed for spontaneous closure, the fistula persist, an incision, such as to lay open any sinuous track, vivify callous edges, or remove spongy granulations or calculous deposits, must be tried. The injection of iodine solution sometimes will stimulate the sinus to healthy action.

If the other kidney be sound, and a permanent fistula communicating with a diseased organ, threatening the life and sacrificing the comfort of the patient, resist other treatment, the best plan is to perform nephrectomy.

Renal fistula opening into the stomach.—This is of extremely rare occurrence. In one case of communication of the left kidney with the stomach, pus urine and calculi are said to have been vomited; but there is much uncertainty as to the genuineness of the symptoms and the accuracy of the diagnosis. In a case of gastro-renal fistula due to scrofulous pyelonephritis, admitted under my care into the Middlesex Hospital in 1884, there was a history of "inflammation of the bladder" and of "pus in the motions," as well as in the urine. There were four sinuses in the back discharging pus. Careful examination of the chest and abdomen disclosed nothing abnormal. No physical signs of pelvic cellulitis or circumrenal abscess could be made out. Complete anuria preceded death. On post-mortem examination the only communication between the kidney and the gastro-intestinal tract was a fistula of the diameter of a crow-quill, opening into the left margin of the great curvature of the stomach.

Renal fistula communicating with different parts of the intestine, and renal fistula opening into the lung, are of very rare occurrence. Prompt surgical treatment might in some instances have prevented their formation.

Ureteral fistulæ are almost invariably the results of operation wounds.

PERINEPHRITIS AND PERINEPHRIC ABSCESS

Perinephritis is inflammation of the cellular and adipose tissues surrounding the kidney. It may occur at any age, having been met with in quite young children; it appears in three forms: the sclerosing, the fibro-fatty, and the phlegmonous.

The sclerosing variety results in the formation of a thick white firm fibrous capsule, which occupies the site of the circumrenal fat and may also extend into the neighbouring parietes in the lumbar region, even to the skin. This sclerosis of the adipose tissue round the kidney leads to compression of the vessels and subsequent atrophy; the organ having been removed in some cases without there being any necessity to ligature the contracted vessels.

The fibro-fatty variety consists in the over-development of the normal envelope of the kidney associated with a certain amount of induration, so that the organ may be concealed in large masses of fat and fibrous tissue which may even penetrate into its substance, rendering its recognition extremely difficult.

The phlegmonous form, which constitutes perinephric abscess, includes all kinds of pus-formation in these tissues. It is rare before puberty.

Perinephric abscesses are: (i.) *Primary* extrarenal abscesses, or those which are independent of any fistulous opening into, or other disease of the kidney. These may depend upon injuries, chills, etc., or may follow the acute exanthems; or the abscess may have extended from a distant part, as the spine, pelvis, etc.

(ii.) *Consecutive* extrarenal abscesses; in which inflammation of the kidney has spread to the cellulo-adipose tissue (*a*) by contiguity, but without urinary infiltration; or (*b*) as a result of a renal fistula communicating with the surrounding cellulo-adipose tissue. This form is usually due to suppurative pyelitis; or to tubercle, cancer, hydatid or other form of cystic disease; or to calculus of the kidney.

(iii.) Consecutive to disease of an organ other than the kidney, as of colon, testis, liver, or one of the pelvic organs.

The pus is situated usually behind the kidney or at one or other extremity of it. In the latter varieties it lies between the kidney and the diaphragm; or between the kidney and the colon, with a tendency to extend towards the iliac fossa. In most instances extension takes place so that all these sites are occupied at once, and the limiting wall is made up of the neighbouring viscera agglutinated together and protected by false membranes, while the enclosed area is broken up into separate suppurating foci. The contents may be thick creamy pus or a thin serous or glairy fluid, often with a feculent odour; and in the midst may lie the immediate cause of the abscess in the form of calculi, hydatids, or intestinal matters. The kidney may be free from disease or may contain suppurating points, not necessarily in direct communication with the abscess, but often situated immediately beneath the capsule, and sometimes constituting the proximate cause of the abscess.

Suppuration may extend to the liver, spleen, or pancreas, and the intestine may be closely adherent; but the peritoneum is rarely involved beyond being adherent and thickened.

In one case, recorded by Coupland, the pleura and lung were involved and the pus was discharged by a bronchus. In others pyothorax has resulted. Below, the abscess has extended to the pelvis and found vent through one of the various natural openings or into one of the pelvic viscera, or has tunnelled along the psoas muscle. Posteriorly it may open superficially in the loin through the triangle of Petit.

Symptoms.—These vary with the cause and acuteness of the disease. When the inflammation is secondary to some distant disease, such as pelvic cellulitis, the symptoms of the primary affection may disguise those of the perinephritis. Extensive sclerosis gives a firmness and immobility to the circumrenal tumour which, taken in conjunction with its position and relations, are quite characteristic.

The constitutional indications of pus in the circumrenal connective tissue are the same as those excited by deep-seated suppuration elsewhere. The febrile temperature in some cases runs continuously high; in others it is intermittent and suggestive of malaria or pyæmia. Obstinate constipation is almost invariable.

Of the local symptoms, those due to pressure are more marked in perinephric abscess than in perinephritis. Pain, deep-seated and often paroxysmal, ushers in the disease; sometimes dull and aching, at others darting, it courses along the distribution of the lumbar plexus. The pain is greatly intensified by bi-manual compression of the loins.

The affected side will impart a sense of increased resistance and weight long before pus has formed, or the abscess is large enough to alter the contour of the part in any way. The skin in the loin is often waxy and œdematous. Fluctuation is frequently very remote, owing to the thickness of the parietes; and in one case, in which six pints of pus were pent up, on account of the great depth of the subcutaneous fat no fluctuation could be detected. Œdema of the foot and ankle has preceded for many weeks every other sign of perinephric abscess. A peculiar lameness, due to the flexed position in which the thigh of the affected side is retained in order to relieve tension, is often an early symptom. There is usually also disturbance of the digestive organs manifested by anorexia with nausea and vomiting, and either diarrhœa or constipation.

In perinephritis before suppuration has occurred the spinal column is preternaturally stiff, and the body in walking is inclined to the affected side; stooping is difficult; in the recumbent posture the patient will not extend the corresponding thigh beyond 160°, or in severe cases 130°; and there is sometimes pain in the knee. These conditions together cause the case to resemble the second stage of hip disease, especially when the thigh is rotated outwards, so that the heel of the affected side during standing rests on the dorsum of the opposite foot. In simple perinephritis there is no tumefaction to be felt in the loin, as in perinephric abscess.

Prognosis.—In a few cases perinephritis ends in resolution before the suppurating stage has been reached. When suppuration occurs, the prognosis depends chiefly on two things, the early and free evacuation of the pus, and the cause of the disease.

When the abscess is primary, that is, not dependent upon renal or other visceral or spinal disease, an opening into it is soon followed by convalescence. If the abscess burst into the peritoneum, rapidly fatal peritonitis ensues.

The abscess may open through Petit's triangle; or by way of the pleura, lung, or pericardium above; by the groin or pelvis below; forwards beside the umbilicus; or inwards by the intestine. In any case the persistence of sinuses and the establishment of lardaceous disease usually lead ultimately to a fatal result.

Etiology.—Perinephritis is most commonly secondary to a suppurative lesion of the kidney. It may, however, arise primarily in the cellular tissue; or be secondary to suppuration in some neighbouring organ; or propagated from some distant one, such as the uterus or cæcum. Perinephritis occurs more often in men than women; it complicates the specific fevers, septic diseases, and puerperal fever. It occurs also after exposure to cold, and in some cases after operations on the lower genito-urinary organs, independently of any affection of the kidney. Among local causes are contusions, strains, and wounds, including infection from an unclosed ureter after nephrectomy for pyonephrosis. The greater number of instances, however, are secondary to disease in the kidney.

Arising by infection from neighbouring organs, circumrenal abscess may be secondary to biliary or intestinal calculus, perforation of the colon, pneumonia, empyema, or pulmonary abscess; infecting virus being conveyed by the veins or lymphatics.

Diagnosis.—The affections which may be mistaken for perinephritis or perinephric abscess are lumbago, various organic diseases of the kidney, spinal caries, splenic tumours, fæcal accumulations in the colon, morbus coxæ, and psoas abscess.

The high situation of the pain; the tenderness in the loin; the fact that passive flexion is painless in itself; the free, painless mobility of the hip-joint; the absence of tenderness and fulness over the upper end of the femur; absence of pain on percussion of the thigh, and the less rigidity of the adductors and rotators, serve to distinguish perinephritis from hip disease.

The symptoms of perinephritis are very closely allied in many points to those which accompany appendicitis; but the characteristic feature of perinephritis is that the pain, tenderness, and swelling are first observed and most pronounced in the ilio-costal interspace behind; whereas in appendicitis they are most frequently located in the iliac fossa and in front.

Treatment.—Primary perinephritis may sometimes be checked in its early stages by local blood-letting by means of leeches or the cupping-glass, hot baths, and hot emollient poultices or stupes.

When the acuteness of the symptoms has passed, or the inflammation is of the subacute or chronic character, disappearance of the inflammatory products may follow blistering, or hot fomentations applied over some absorbent ointment such as iodide of potash or iodide of lead. The bowels should be well opened at the onset by a brisk purgative, and kept acting moderately by enemas or mild laxatives.

Pain must be relieved by morphia given in suppository or by the mouth. The diet should be milk, beef-tea, or something equally simple and as readily digested.

As soon as pus is suspected, it should be searched for at once by an exploratory incision in the loin; and when found must be evacuated by a free incision in this region.

There should be no waiting for fluctuation; the increasing fulness, hardness, and tenderness, and perhaps the commencing redness and œdema of the skin, are ample signs to warrant an incision, and even to demand it. Trousseau, among others, pointed out the difficulty of detecting fluctuation, which he says is almost always deep, requiring great experience to make out; but the doughy feel of the lumbar region, the increase of the fever and other general symptoms, and perhaps the œdema of the skin in the loin, are indications for a free incision which the surgeon must not hesitate to act upon with promptitude.

The incision may be either vertical, oblique, or transverse; and after dividing the integument and muscles with the knife, the suppurating area should be entered by the finger. The abscess cavity and kidney should be examined with the finger in search for a stone; should a renal fistula exist, it must be laid open, especially if the preceding symptoms indicate calculous pyelitis.

Any loose sloughs of cellular tissue should be removed by the finger or dressing-forceps. The abscess should be washed out with a solution of iodine or carbolic acid, and a drainage-tube should be inserted.

The loin should then be enveloped in a large hot fomentation of cotton-wool soaked in equal quantities of water and carbolic acid solution (1-40); or, if there is redness or œdema, equal parts of lead lotion and carbolic acid solution (1-40). Absolute rest in bed should be enforced throughout convalescence.

Consecutive abscesses, and also some of the less acute forms of primary abscess which do not soften down very quickly, must not be allowed to close too early. On the contrary, the drainage-tubes should be retained until, by the granulating process in the wound, they are forced out by degrees. If in these cases the wound is allowed to close too early, inflammation recurs and pus is formed afresh, which will need a second incision to prevent burrowing far and wide. When a fistulous opening remains, astringent or iodine solutions may be injected, or the hot wire introduced; but a fistula may persist in spite of the most persevering measures employed to close it. A lumbar hernia may follow the incision for the evacuation of an abscess, or for the examination of the kidney, but excessively rarely does so.

Whilst suppuration continues, nutritious food, tonics, and possibly a regulated allowance of stimulants should be given. The record of cases in which early and free evacuation of pus has been accomplished is very favourable, nearly all ending in recovery. On the other hand, perinephric abscess left to itself almost always ends fatally; except in the rare instances in which the matter finds vent by the bowel, bladder, or bronchi, or opens externally.

TRAUMATIC NEPHRITIS

Causes.—Wound or contusion of the substance of the kidney, violent muscular strain, the contusions caused by the presence of a calculus. When blood has been extravasated into the cavity of the kidney, and the urine retained there in consequence of impaction of a blood-clot in the ureter, pyelitis and pyelonephritis may arise.

Symptoms.—Rigor; fever; pain not constant, and very variable in degree, deep-seated and referable to the loin, sometimes diffused over a considerable area of the abdomen, and rarely of a throbbing character unless the perinephric tissue be also involved. Nearly all movements aggravate the pain. If the disease sets in soon after an injury, the urine always contains a trace of blood. Subsequently, in a few cases, pus may be found in the urine.

There is a disposition to the formation of gravel and calculus—and, as a consequence, to renal colic—after wounds or concussions of the kidney.

Traumatic nephritis is not usually serious, provided the damage inflicted on the kidney be not great and the large vessels be not ruptured. If severe, the kidney may be softened into a mere pulp.

Treatment.—If the pelvis of the kidney has been penetrated, urine will drain away by the external wound. If the organ has been opened by subparietal laceration or rupture, the chief danger when the large vessels are uninjured is from infiltration of urine mixed with blood into the cellular tissue. Then it may be necessary to lay open the loin by a free incision down to the injured kidney, so as to provide for the free drainage of the extravasated urine and inflammatory products.

When there is no extravasation, small quantities of fluid diet, the application of cold or leeches, relief of the bowel by one good purgative dose or an enema, and opium to relieve pain constitute the usual necessary details of treatment.

SUPPURATIVE NEPHRITIS, PYELITIS, AND PYELONEPHRITIS

One of the most frequent of the secondary affections of the kidney (secondary, that is, to obstruction to the outflow of urine, to reflex irritation, or to decomposition of urine in the bladder) is suppuration in the pelvis, or in the substance of the kidney, or in both.

In by far the greater number of such cases chronic dilatation of the pelvis and calyces precedes suppuration of these parts; and, later, numerous small scattered abscesses occur throughout the renal substance.

It is to this general affection of pelvis and substance of the kidney from obstruction in the lower urinary passages, or disease of them, that the name suppurative pyelonephritis has been given. It is to this condition that the name surgical kidney has also, but very inaptly, been applied.

Suppurative nephritis, or, in other words, "acute interstitial nephritis, with scattered points of suppuration," occasionally occurs alone, without any affection of the ureter and pelvis of the kidney; this, however, is not commonly the case. Usually acute pyelitis and suppurative nephritis exist simultaneously; but if suppurative nephritis happen to be uncomplicated with pyelitis, the nephritis is prone to be overlooked, because then the urine contained in the pelvis of the kidney, and drawn off by a catheter immediately after washing out the bladder, is acid and without the odour of decomposition. Nevertheless the temperature and other constitutional symptoms ought to correct the fallacy.

Etiology.—Infective lesions of the kidney may arise from the upward extension of inflammatory affections of the lower urinary apparatus, which are by far the most frequent cause of them. In other cases the infection is conveyed to the kidney directly by the blood-vessels, and thence descends along the ureter to the bladder: these are much less common.

A more important distinction consists in the presence or absence of distension of the renal pelvis. Pyelonephritis without distension admits of medicinal treatment, and shows itself by high temperature and other symptoms; pyelonephritis with distension manifests itself by definite physical signs also, and, generally speaking, needs surgical methods.

In the causation of suppurative disease of the kidney the influence of sex is prominent; the very much greater number of cases occurring in men being consequent upon the greater frequency of diseases of the bladder in them; whereas in women similar changes occurring in the kidney are usually associated with morbid conditions of the utero-ovarian system. Arterio-sclerosis, associated with interstitial nephritis and enlargement of the prostate, is a frequent predisposing cause of bacterial infection of the kidneys in men. In women such infection results from intrapelvic compression of the ureters resulting from fibroma, cancer, peritonitis, or prolapse of the uterus.

Renal congestion, due to reflex changes in connection with cutaneous impressions, over-distension of the bladder and particularly to the vaso-motor paralysis accompanying injury to the spinal cord, is an important predisposing cause, to which may perhaps be added the influence of albuminuria and defective nutrition of the tissues.

Among exciting causes may be mentioned pyæmia and puerperal fever (which more often induce abscess of the kidney than pyelonephritis), and the allied blood conditions which accompany erysipelas, burns and osteomyelitis. Of the more immediate local causes are injuries to the kidney or ureter, pelvic cellulitis, cystitis due to septic catheterisation, and frequent over-distension of the bladder from various causes.

Pathology.—The ascent of micro-organisms to the kidney is assisted by the failure of peristaltic contraction and the dilatation which are associated with retention of urine; and again by the contractions of the bladder which are provoked by the obstruction to the natural escape of its contents.

Congestion of the kidney renders it more vulnerable on the entry of micro-organisms; these develop more readily in an albuminous fluid, and the arrangement of the blood and lymphatic vessels of the kidney and ureter affords a direct means of invasion in cases of urethritis. Ureteritis leads sometimes to thickening and sometimes to dilatation of the tube, and in a few cases to a sclerosis of the vesical extremity with impairment of the valve-action there. The pelvis of the kidney is subject to similar pathological changes, the walls being either thickened and contracted or thinned and dilated. In acute inflammation the mucous lining is vascular and swollen, covered with glairy muco-pus or false membrane, a deposit of phosphates often being added.

Without distension, the kidney may be enlarged, soft, œdematous, grayish in colour, and showing no distinction between cortex and medulla. The parenchyma may contain cysts, collections of fat, and (in the acute cases) miliary abscesses or areas of necrosis.

With distension of the pelvis and calyces, the kidney may attain the size of the human head. It is closely attached to the neighbouring organs, tissues, and vessels. The fatty envelope is usually sclerosed and adherent, as is also the capsule. A quart or more of pus may be contained in the cavity and all appearance of the gland substance may be lost, nothing remaining but an apparently fibrous membrane with septa completely or incompletely dividing the cavity. The lining membrane is continuous with that of the ureter, and often ulcerated or gangrenous. In other cases many separate abscesses of the renal substance may be present, and the cavity of the pelvis may be occupied by primary or secondary calculi.

Microscopically the substance of the kidney may display disseminated, cortical, or radiating medullary abscesses, with granular and fatty changes in the convoluted tubes, and proliferation of the epithelium of the glomeruli, accompanied by general hyperæmia and the presence of hæmorrhages; in chronic cases sclerosis and suppuration may be found.

Symptoms.—These are wasting, loss of appetite, furred tongue, and disturbed digestion and loss of strength. The skin becomes dry, pale or jaundiced. There is more or less fever. The symptoms, however, exhibit wide variations, and in some cases are so slightly marked that they attract no notice.

The acute form is ushered in by fever and rigors often accompanied by delirium; emaciation with severe disturbance of the digestive functions and sweating ensue. The disease may prove fatal by hyperpyrexia or exhaustion in this stage, but more often lapses into the chronic form. This, however, may be established without the initial acute phase. The bulk of the symptoms then are manifested by the digestive system, so that most of the patients are regarded as dyspeptics; and this mistake is the more likely, as the temperature is but little raised. The mouth and pharynx are dry, owing to deficiency of saliva, speech and deglutition are interfered with, and the patient will swallow nothing but liquid. There are vomiting, flatulence, tympanites and commonly constipation, though this last may give place in the later stages to fœtid diarrhœa.

The patient suffers much from cold, from great depression, and muscular weakness. Walking becomes difficult, and the inability may amount almost to paraplegia. Sleep is disturbed, and there may be nocturnal delirium. The skin is dry, cold, and rough, with detached epidermal scales; it is often irritable and affected with various eruptions. The circulatory system is commonly not affected, until in the latest stages of the affection the heart becomes weak and irregular. In cases of a mild form the symptoms are little marked, and the patient may be able from time to time to resume his occupation. Nevertheless, progressive loss of flesh and strength and congestion of the internal organs, especially of the lungs, become apparent, and the patient is liable under the influence of chills or fatigue to manifest the more acute symptoms, or to relapse ultimately into the more severe chronic condition mentioned above, dying of urinary cachexia without actually presenting the definite symptoms of uræmia.

Locally the signs vary according as there is pyelonephritis with or without distension, and according as this is permanent or intermittent. There is pain in the region of the kidney, and tenderness on deep palpation, or pain elicited by movement when calculus is present. Pyelonephritis without distension occurs mostly in old people, often in the course of chronic cystitis, and directly on exposure to chill or catheterism. The onset is marked by fever, or may supervene gradually with pain in the lumbar region and polyuria, accompanied by albumin and casts. The daily secretion of urine is increased to from four to eight pints. It is pale and of low specific gravity, and presents a grayish-white deposit of pus with a supernatant cloud of mucus or liquor puris on standing. On expulsion, the urine is uniformly opalescent or may be slightly denser towards the end of micturition; early in the disease it has an acid reaction, but later it becomes neutral or alkaline.

The urea is diminished, albumin is present independently of the pus, and the tendency to putrefaction and ammoniacal change is more marked than in healthy urine. Slight hæmorrhage occasionally occurs; but when it is abundant, and influenced by movement, it probably depends on the existence of a renal calculus.

Microscopical examination reveals epithelial cells derived from the tubules, hyaline casts, and casts made up of pus cells, imbricated epithelium from the pelvis and sometimes fragments of renal tissue, triple phosphate crystals, and various forms of micro-organisms.

Pyelonephritis with distension, which may ensue, is characterised by the presence of a renal tumour and by intermittence of the pyuria. The swelling is generally smooth and rounded, occupying the loin and yielding a resonant note on percussion in front. There is pain and tenderness, and very often perinephritis supervenes, increasing the size and firmness of the swelling.

With the appearance or increase of the tumour there may be disappearance or diminution of pus from the urine; and when the tumour subsides, pus reappears in increased quantity, and the symptoms are temporarily alleviated The further course of the case may be that of pyonephrosis; or of renal abscess complicated by secondary calculi, with pain and hæmorrhage on movement; or of perinephritis either of the sclerosing or suppurative variety, the severity of the symptoms being accentuated by the probable implication of the opposite kidney.

Diagnosis.—When no tumour exists, but only constitutional symptoms, with pyuria, the disease may easily be confounded with chronic cystitis, or with tuberculosis of the urinary organs. In chronic cystitis there would probably be no polyuria, the urine would be alkaline and glutinous, and the distribution of pus in the urine would be less uniform than in pyelonephritis.

Tuberculous disease of the kidney is usually associated with recognisable lesions in other organs, and the characteristic bacilli may be found in the deposit in the urine. Hæmorrhage is more frequent, and the febrile exacerbations are less marked. The rapid failure of the patient's strength is sometimes an important sign.

When a tumour is present, the disease may simulate tuberculosis or hydronephrosis; in the latter case fever and septic manifestations are usually absent.

Prognosis.—Attacks of the primary affection due to irritant drugs, such as cantharides, or to cold, are usually transitory. Those that follow disease of the bladder or other pelvic organs, those affecting both sides, and those that develop acutely, are more formidable, threatening death by urinary toxæmia. Chronic cases with free discharge of pus have the most extended course, lasting often for months or years; and the outlook depends largely on the condition of the digestive organs.

The most formidable cases are those of retention of pus, which distends the renal pelvis and destroys the parenchyma, leading to toxæmia or to the rupture of the sac and the establishment of a fistula.

Treatment.—In suppurative nephritis and pyelonephritis the treatment is essentially the same as that for acute or subacute nephritis without suppuration. Every precaution should be taken to prevent their recurrence. Any obstruction to the outflow of urine, or any incapacity to empty the bladder completely, should be remedied or counteracted; stricture of the urethra should be dilated or divided, vesical calculus removed, and the effects of enlarged prostate combated by early and regular catheterism. If chronic cystitis exists, daily irrigation of the bladder will be necessary to obviate decomposition of the urine and to restore the mucous membrane to a healthy state. The impaction of a stone in its course between the kidney and bladder calls for its removal either by the bladder, loin, or abdominal route; according to its position in the ureter. Confinement to bed is necessary as soon as inflammation has once set in.

With the object of avoiding the severe and dangerous onset of pyelonephritis, as well as the slighter forms of urinary fever, catheterism should never be employed except when the patient during and for some hours after the introduction of the instrument is in a warm and equable temperature, preferably in his bed.

The bowels should be kept well opened, and for this purpose warm abundant enemas are of special service.

The diet should be light and moderate, and should consist chiefly of fish, milk, chicken or game, light farinaceous or milk puddings, and well-cooked vegetables; uncooked vegetables and fruits as well as butcher's meat should be avoided. Stimulants should be taken, if at all, in very small quantities; and if, during their administration, the pulse is quickened, the temperature raised, or the urine becomes more purulent, they should be discontinued at once.

Liquids should be taken in moderate quantity only, if the amount of urine secreted be abnormally large; but where cystitis exists, and much mucus is passed in the urine, barley water, triticum repens, and linseed tea are useful adjuncts in slaking thirst and relieving the irritation of ammoniacal urine.

Little can be said in favour of medicines; a mixture of one grain of quinine with 5 min. of tincture of opium and 20 grains of citrate of potash in mucilage has proved of benefit in some cases; and 5 grains of salol or biborate of magnesia in doses of ½-1 drachm have been given, with a view of controlling the septic changes in the urinary tract. When constipation exists, and a large quantity of urine is secreted, I have seen great benefit accrue from a few doses of ergot of rye. This drug, by acting upon the involuntary muscle fibres of the gut, overcomes the constipation, and by its influence on the coats of the blood-vessels constricts and gives tone to the renal circulation. The constipation, flatulence, atony of bladder, and general arterial and muscular feebleness, suggest remedies which will give contractile force to the muscular fibres of the viscera.

When the febrile attacks take the remittent form, 5 gr. of quinine in 1 oz. of lemon juice, and ½ drachm to 1 drachm of liquor morphinæ, are sometimes very efficacious in checking the rise of temperature.

Traube obtained good results from injections into the bladder of acetate of lead, from ½-1½ gr. in 4 oz. of distilled water, and the internal administration of pills of tannic acid (1-1½ gr.) every two hours. He recommends both of these remedies because of their antiseptic and antiphlogistic action.

Drugs like tannin, alum, acetate of lead, and perchloride of iron, which act as astringents upon the blood-vessels of the mucous membrane, and so lessen the excessive secretion of mucus, have been recommended, and certainly deserve fair trial. When the urine is alkaline, benzoate of ammonia in 10-grain doses may be tried and often with benefit.

Renal Abscess

Abscess of the kidney is one of the varieties of suppurative diseases of the kidney. It is not intended here to refer to any of those forms of suppurative nephritis characterised by the development of minute and scattered points of pus, the origin of which may be infection carried by the ureter, vessels, or lymphatics; nor is it intended to include miliary abscesses due to the irritation of calculous matter in the kidney or to the decomposition of urine in the renal pelvis resulting from any of the numerous causes of obstruction to the outflow of urine. What we have now to describe is that form of suppuration which results in the formation of one or more abscesses of considerable size in the substance of the kidney.

Etiology.—It must be stated at once that renal abscess of large size, involving the greater part or even the whole of the kidney, occurs as the result of the fusing together of a large number of miliary abscesses. Suppuration of this kind may be limited to one kidney, the other being quite unaffected. Metastatic and secondary abscesses of large size may be also formed otherwise. Thus, in pyæmia, or in cases of embolism derived from ulcerative endocarditis, instead of a number of minute and scattered emboli followed by minute and scattered points of inflammation and suppuration, one large vessel may be obstructed by an embolus and a large abscess may ensue. Sometimes, as a result of stricture or other disease of the lower urinary organs, a circumscribed abscess may form in the tubular substance of the kidney. Wounds, contusions, and lacerations of the kidney, and kicks, blows, or falls, involving the loin or renal region on the front of the abdomen, are occasional causes of suppuration and abscess of the kidney. More usually when renal abscess occurs as the result of injury to the loin, whether attended with immediate injury to the kidney or not, the suppuration of the kidney has been preceded by suppuration in the circumrenal cellular tissue; so that the abscess involves the kidney by spreading from without, and is not primarily a renal abscess. Injuries which cause obstruction in the renal pelvis or ureter are especially likely to be followed by more or less suppuration of the renal tissue; moreover, injury to the kidney, from its tendency to excite the formation of renal calculus in the injured organ, may be in this way an indirect cause of renal abscesses of large size. A calculus which originates in a renal tubule, or one which becomes more or less shut off by inflammatory adhesions from the general cavity of the pelvis of the kidney, is the most likely to give rise to an abscess in the substance of the kidney; the impaction of a stone in the renal pelvis or ureter leads more frequently to calculous pyelitis and thus to pyonephrosis.

Foreign bodies other than calculi may give rise to a large renal abscess. A piece of bone, a fragment of clothing, or a bullet, may gain entrance to the kidney; and, instead of becoming quietly encysted, or passing through the natural channels out of the body, it may give rise to extensive suppuration in the organ in which it rests.

Irritant drugs, such as cantharides and turpentine, have been known to cause renal abscess. A kidney illustrating this change is preserved in the Museum of the College of Surgeons. Cantharides was the drug administered, and death occurred in three weeks.

Pathology.—Circumscribed abscess usually affects one kidney only. There may be one or several abscesses in the same organ. In size, they vary from that of a hazel-nut to that of an orange. They may communicate with the pelvis of the kidney, or through the capsule with the circumrenal cellular tissue. When they open through the capsule they lead either to a circumscribed perinephric abscess, or to diffused and burrowing retroperitoneal suppuration. When they open into the renal pelvis they may empty themselves partially or entirely through the ureter and bladder. When two or more abscesses affect the same organ they may communicate with one another or remain distinct; and one may discharge in one or other direction, the others remaining unopened. This isolation of several abscesses should be borne in mind in exploring the kidney for suppuration.

In a very considerable number of specimens of renal abscess, the whole organ, including the pelvis, is involved; and very little, if any, renal substance is left.

It is not easy in some of these cases, especially when the ureter of the affected side is pervious, and the opposite kidney and lower urinary organs are not diseased, to say whether the morbid process began as a pyonephrosis or as abscess in the renal substance. It is undeniable that many of the cases reported in the journals and elsewhere as renal abscess are really far advanced cases of pyonephrosis.

Symptoms.—These may be either acute or chronic. In the acute cases there is pain in the region of the diseased organ, with fever and rigors. The rigors are sometimes marked and frequent; at other times only one or two occur throughout the course of the disease, and these at uncertain and irregular periods.

Hæmaturia often precedes the formation of abscess when the cause is traumatic. The absence of pus in the urine is no test; in many cases there has been none whatever throughout. In other instances, if the abscess have broken into the ureter or pelvis of the kidney, pus, it may be in large quantity, will be seen in the urine.

If a tumour has been formed in the loin, the discharge of pus by the bladder will probably be followed by diminution or subsidence of the tumour. It is not often, however, that any tumour perceptible during life is formed by a circumscribed abscess of the renal substance. If a tumour do exist, with the history or symptoms suggestive of suppuration, dilatation of the cavity of the kidney may with fair certainty be predicted; or else it may be that the whole organ is in a state of general inflammation with several foci of threatening or actual suppuration.

When the abscess is chronic in character, it forms without causing any definite symptoms. Indeed, the abscess may be found at the post-mortem examination without having caused a suspicion of its existence during life. In some cases, however, general impairment of health, occasional chilliness and rigors, obscure aching in the loin, gradual emaciation and increasing sallowness or duskiness of skin indicate some grave disorder, but do not point with any distinctness to its nature.

In acute cases a fatal termination may occur in a fortnight to three weeks. The cause of death will most probably be typhoid prostration. Occasionally, however, the abscess bursts into the cellular tissue, the intestine, or the renal pelvis or ureter; and then life may be prolonged for a time, till ended by exhaustion or hectic.

Possibly recovery may ensue; in some cases it is pretty certain that the contents of the abscess, instead of escaping in any of the directions mentioned, become inspissated and remain quiescent for the rest of life.

Treatment.—The treatment of the early stages of a renal abscess will depend largely on the cause. If it be due to external violence, restricted diet and fluids, rest, anodynes, leeches, or cupping on the loin, the application of an ice-bag, and, after the first day or two of the inflammation, the constant application of hot fomentations, is the treatment that must be followed. If caused by renal calculus, the treatment suitable for the varying phases of this disease will be required. In any case in which there is clear indication of a renal abscess, the pus ought to be evacuated through an incision in the loin.

Indeed, in the absence of a tumour, but with the history and symptoms suggestive of suppuration, to make an exploratory incision down to the kidney is the right treatment. If, when the kidney is punctured, pus is found, it is not sufficient to evacuate it with a trochar and canula; a free incision should be made into the abscess, and the wall of the abscess cavity, if a large one, should be stitched to the edge of the wound. When the finger in the kidney enters a space which does not communicate with the general pelvic cavity of the organ, or does so only by a small orifice, the rest of the surface of the organ should be carefully manipulated, and if fresh pus be found, a second or even a third incision of the renal substance should be made so as to open the other abscesses. If the kidney be very much destroyed, it may be best to remove it at once through the lumbar incision.

The kidney is very much more tolerant of interference than it is generally believed to be; and the fear of hæmorrhage is reduced to a minimum by restricting incisions to the periphery. In cases where nephrotomy has revealed either local or disseminated disease with areas of healthy parenchyma between the foci, and especially if there be a probability of bilateral distribution, it is better, instead of removing such a kidney, to treat each focus independently by scraping or by the excision of a wedge. This plan may be resorted to in cases of multiple abscess or of multiple tuberculous deposit, and may be combined with nephrolithotomy. When operative measures have to be taken in connection with the second kidney, the surgeon has a much freer hand if the active and healthy part of the organ first operated upon is still discharging its function.

It is remarkable, too, what a powerful influence on the secretion of urine even small portions of renal substance exert, and what a capacity for recovery they evince after the removal of some condition interfering with their functional activity; such as pressure, or obstruction of the ureter. Evidence of this is met with in the quantity of urine (often of low specific gravity, it is true) passed after relief of hydronephrosis, where the organ has been distended and thinned to a mere capsule; and not frequently at necropsies mere remnants of kidneys, weighing but a few drachms, are found, which had been active and serviceable for many years between the occurrence of acute disease and the ultimate death of the patient.

HYDRONEPHROSIS

This name is given to over-distension of the kidney with urine, the result of mechanical obstruction, no matter whether the cause be in the urethra, bladder, or ureter. Probably one-third of the cases of hydronephrosis in which a palpable tumour is formed have a congenital origin.

Congenital causes.—Twistings, undue obliquity, contractions, and other anomalies of the ureter. This duct is in some cases a mere fibrous cord; or its vesical orifice may be of pinhole size; or minute cysts may be developed in its mucous membrane; or the angle of its junction with the kidney may be so acute as to impede the descent of the urine.

Acquired causes are cancer of the pelvic organs, fibro-myoma, pelvic inflammation with contraction of the cellular tissue. On account of its frequent dependence on pelvic disease and upon movable kidney, hydronephrosis is very much more frequent in women than in men. Calculus, either by its impaction in the ureter, or by the ulceration and subsequent contraction at some spot in this tube excited by its passage to the bladder, is a frequent cause. Other causes are inflammations, tumours, or abscess of the bladder causing contraction of the vesical orifice of the ureter. A papilloma of the bladder has been the cause; or, again, enlarged lymphatic glands, adhesions or bands of fibrous tissue, enlarged prostate, and stricture of the urethra. Hydronephrosis may affect both kidneys or only one, or may be limited to a part of one kidney. Cases of double hydronephrosis of congenital origin are not very uncommon. The proportion of cases in which hydronephrosis produces a palpable abdominal tumour is very small compared with the frequency of the disease.

Pathology.—The pelvis of the kidney first becomes converted into a spheroidal sac, then the calyces are widened and stretched in every direction, and at length the capsule of the organ is expanded, and what remains of its cortical and medullary substance becomes still further compressed and absorbed until nothing is left but a loculated cyst, the septa of which are inextensible. The size of the hydronephrotic sac may not exceed that of a normal kidney, it may even be smaller; or, on the other hand, it may be sufficiently large to form a swelling occupying a great part of the abdominal cavity. The contained fluid is water holding a larger amount of sodium chloride than exists in urine and a few epithelium cells. Its quantity is sometimes enormous, reaching several gallons. Urea is often all but absent. The reaction is acid or neutral, and it may be dark in colour and colloid in consistence. When the seat of obstruction is in the lower urinary organs the ureter is dilated, and commonly the change is bilateral. When the obstruction is in the urethra, purulent infection is more common, and pyonephrosis succeeds to hydronephrosis. As regards the communication with the bladder, it may be open, closed, or valvular.

My experience in operations on the kidney has led me to classify cases of hydronephrosis into (i.) Simple hydronephrosis with atrophy without expansion; these are the small, flaccid, shrivelled kidneys: (ii.) Simple hydronephrosis with atrophy and expansion; these often enlarge into huge cysts: (iii.) Hydronephrosis with atrophy of the pyramidal, and thickening and sclerosis of the medullary substance; these kidneys have generally been the seat of inflammation and are prone to suppurate.

Symptoms.—Hydronephrosis may occur at any age, and is twice as frequent in females as in males. When the dilatation is insufficient to give rise to a tumour, there are generally no signs characteristic of hydronephrosis. Out of a series of 142 cases at the Middlesex Hospital an abdominal tumour was formed in but very few. In some advanced cases in which no tumour exists, thirst, pain in the back, frequent micturition, partial, total, or intermittent anuria, and obscure or pronounced abdominal pains are present.

A hydronephrotic tumour is dull on percussion, sometimes lobulated in contour, and frequently fluctuates. It has all the characters of a renal tumour, being situated in the flank, pressing the ilio-costal parietes backwards and outwards, having the colon in front of it, and the small intestine either in front or thrust over to the opposite side of the abdomen, according to the bulk of the swelling. If of no great size, it may be painless; if large, it may give rise to excruciating suffering.

When it arises from some innocent cause, such as pregnancy or uterine flexion, its formation is unattended by any constitutional or local disturbance; but when from some painful cause, such as impacted calculus, or sudden kinking of the ureter, the symptoms incidental to the particular condition will occur before the tumour makes its appearance, and may cause it to be overlooked.

There are instances of the tumour *intermitting*, that is, being prominent at one time and not distinguishable at another, the disappearance of the tumour being sometimes associated with polyuria, the urine being accompanied by blood, pus, or mucus. In some cases constipation results from pressure on the colon; in others, no recognisable symptoms occur till uræmia sets in.

Diagnosis.—When of moderate size, the tumour has to be distinguished from renal or perinephric abscess and perinephric extravasation. When it forms a palpable tumour, it may be mistaken for pyonephrosis, or for a hydatid or serous cyst of the kidney, liver, or spleen. When of great size, it may simulate ascites or parovarian cystoma. If the subsidence of the tumour is followed by an increase in the outflow of urine, the diagnosis of its hydronephrotic nature is well-nigh certain. Perinephric abscess is quicker in its course, and excites much more pain and constitutional trouble in its early stage. Between hydronephrotic and pyonephrotic tumours the diagnosis is often impossible and indeed immaterial.

Purulent urine, rigors, and fever indicate pyonephrosis as a rule; but such diagnostic symptoms may be absent. Hydatid and serous cysts of the kidney are best diagnosed by their history.

From ovarian tumours the diagnosis is often very difficult. These are, as a rule, more mobile than renal cysts, and enlarge upwards from the pelvis, not forwards from the loin. Moreover, the intestines are behind an ovarian and in front of a renal tumour. When the tumour is renal, the uterus is neither displaced nor fixed. In the case of an ovarian or parovarian cyst, on the other hand, it is displaced upwards and to one side.

Prognosis.—This depends in great measure upon the distension, but chiefly upon whether one or both organs are involved. If only one kidney is affected, and the tumour not large, life may be indefinitely prolonged. There is always, however, the fear that calculus or other disease of the opposite kidney may cause death by suppression of urine or uræmia; or that suppuration may occur in the cyst. If the distension increase, death may result from pressure on neighbouring organs, rupture into the peritoneum, or suppression of the urine.

Treatment.—Medical remedies are of no avail. Surgical measures should be directed against the cause of the hydronephrosis, whether it be in the pelvis or due to the mobility of the kidney. When of small size and painless, these hydronephrotic tumours may be left alone. When they cause trouble by pressure, they should be treated by nephrotomy or nephrectomy.

Regular friction of the tumour has proved successful, in at least three cases, by overcoming the obstacle to the passage of the urine, and so in emptying the cyst into the bladder. If paracentesis be decided upon, and there is nothing to indicate any spot for puncture, the best point to tap a tumour of the left kidney is just anterior to the last intercostal space; but if the right kidney is affected this is too high, and the puncture should be made half-way between the last rib and the iliac crest, and two inches behind the anterior superior spine of the ilium. Repeated tappings will probably be required. Nephrotomy is the proper operation, and should be preferred to aspiration. Drainage and antiseptic irrigation are effected by means of a large rubber tube, which should be fixed in the cyst.

After nephrotomy for hydronephrosis search should be made with the finger through the lumbar incision with the object of detecting a stone, and the ureter should also be tested by passing a long probe or small sound along it from the interior of the kidney downwards. Lumbar nephrectomy is required when the kidney is so much damaged as to be incapable of performing its function, or where there is a free continuous discharge from the loin after treatment by nephrotomy; except in cases where the opposite kidney is defective.

CONGENITAL HYDRONEPHROSIS.—In by far the larger number of cases of hydronephrosis found in the fœtus and new-born, both kidneys are involved; the most common cause being imperforate urethra. It may be due to minute cysts, to membranous septa in the urethra, or to cysts in the ureter or pelvis of the kidney. The subjects of this disease may be born dead, or may live for a few weeks, months, or even years.

The urine removed from some of the cases of congenital hydronephrosis has contained little or no urea. The size of a hydronephrotic fœtus has proved a serious impediment to labour in several cases, and has rendered parturition impossible, until the abdomen of the child has been reduced by tapping.

Congenital hydronephrosis is frequently associated with some other congenital deformity, such as hare-lip and club-foot.

These cases prove that the secretion of urine goes on to a very considerable extent during the latter half of intra-uterine gestation; and that when any obstacle to the outflow of urine exists, the same pernicious effects of distension of the bladder, ureters, and kidneys occur before birth as are commonly known to arise from phimosis, urethral stricture, calculus, and other causes of obstruction after birth.

PYONEPHROSIS

This term implies dilatation of the pelvis and calyces of the kidney with pus, or pus and urine. In advanced cases the suppuration and dilatation extend beyond the calyces, and go on to compression and disintegration of the medullary and cortical substance, converting the organ into a large loculated sac, the nature of the contents of which depends upon the cause of the obstruction.

Hydronephrosis becomes pyonephrosis as soon as suppuration occurs; and therefore the causes of pyonephrosis are similar to those which generate hydronephrosis. When an obstruction causes pyonephrosis at once, it is more complete in its character, and more rapid in its irritative effects upon the kidney, than when it causes hydronephrosis first. In some cases of pyonephrosis, the pyelitis, instead of following, has preceded the obstruction. A small mass consisting of blood-clot, inspissated pus or mucus, as a result of pyelitis; or the detritus from a calculus, new growth or tuberculous deposit may block the ureter, and so lead to distension with urine and pus; to which may be added, in some instances, blood, mucus, phosphatic deposit and detritus from the disorganised kidney or new growth.

Etiology.—The most frequent cause of pyonephrosis is calculous pyelitis; indeed, renal calculus is so largely in excess of other causes that it has been implied, if not explicitly stated by some writers, that pyonephrosis and calculous pyelitis, when they assume the dimensions of a renal tumour, are one and the same thing. This, however, is not the case. Definite and even fatal pyonephrosis may exist without giving rise to any palpable tumour during life; and without doubt may be caused by many conditions other than stone. Such other causes are pyelitis from extension of septic inflammation from the lower urinary organs, arising in stricture, gonorrhœa, spinal disease, and cystitis however produced, obstruction of the ureter by pressure or infiltration of tumours or inflammation in the pelvis; tuberculous and pyæmic deposits in the kidney or renal pelvis; the presence of such parasites as Hydatid, and Eustrongylus gigas in rare instances; or the occurrence of direct injury.

Morbid anatomy.—When pyelitis, whether acute or chronic, is associated with retention of urine within the renal pelvis, the mucous membrane by degrees assumes a dull white colour, is markedly thickened, and secretes a quantity of pus. The pent-up urine soon becomes alkaline from admixture with pus, urea is converted into carbonate of ammonia, and calculous material is often deposited upon the lining membrane of the organ. As the distension of the cavity of the kidney proceeds, the orifices by which the calyces and pelvis communicate often become narrow and even entirely closed, the pyramids, and then the cortex of the kidney, become more and more atrophied, until at length all the glandular tissue is completely removed, and the organ is transformed into a multilocular or many-chambered cyst. Its relations and connections with the surrounding structures vary. Sometimes it forms adhesions on all sides. Ulceration of the cyst wall, or suppurating tracts formed through what remains of the renal substance, may end in fistulous openings through which the purulent urine escapes and gives rise to perinephritis, peritonitis, or the discharge of pus and urine by the mouth or rectum, or through the loin.

The fluid contained in the distended kidney is occasionally pus with blood, or pus so concentrated that there is hardly a trace of urine. If it has become changed by decomposition and the development of ammonia, it is more or less thready and glairy; at other times it is a soft mortary material, of a white or buff colour; in other cases it is of the consistence of butter. When a calculus is formed in the kidney, it often assumes a branched form which exactly fits the pelvis and calyces. Sometimes independent calculi occupy the pelvis and calyces. Incomplete and persisting or complete but interrupted obstruction to the escape of urine or pus from the kidney pelvis gives rise to the greatest degree of expansion of the organ. When the obstruction is complete and persistent, the parenchyma of the kidney atrophies rapidly and before the calyces and renal pelvis expand to any great degree. In some cases the kidney becomes completely sacculated, and left without a trace of glandular tissue; subsequently it shrinks to much below the normal size.

Symptoms.—In the early stages the symptoms are those excited by the cause of obstruction, whatever that may be; and in addition those of pyelitis.

If the obstruction be not complete, there will be pus in the urine; if intermittent, there will be times during which more pus is discharged than at others; if complete and permanent, there will be an entire absence of pus in the urine. There will be constitutional symptoms of suppuration, and, when the pyelitis is very chronic, all the characters of hectic. When a tumour forms in one or other loin, it possesses the same characters as a hydronephrotic tumour. It is elastic or fluctuating, or nodulated and hard, and bulging the flank as well as occupying more or less of the abdomen. When the tumour is not of great size, there may be a line of resonance above it, but if it be of considerable dimensions it may have formed adhesions with the under surface of the liver or spleen, and so simulate a tumour or hypertrophy of one or other of these organs. If very large, the tumour has almost always a more or less nodulated or lobulated outline, and the resonance of the distended colon may be elicited on the outer side; when this is the case, and fluctuation is also distinct, hydro- or pyo-nephrosis is clearly indicated. The pain experienced depends greatly on the size of the tumour; in some cases there are paroxysms of great severity. Pressure over the front of the tumour nearly always aggravates pain, or provokes it if it were not present before. Pressure over the flank, in some cases, is not only well borne, but actually gives relief.

When the cause of the obstruction is intermittent in its action, the lumbar tumour will diminish, or may even disappear altogether after the discharge of pus. It is always necessary, therefore, to watch the urine continuously and carefully, having the total quantity passed during twenty-four hours collected and measured.

If the ureter be completely blocked, the total quantity of urine excreted, for a short time at least after the occlusion, will be markedly diminished in quantity. If partially blocked the quantity of pus and urine will vary from time to time, even during the same day; and if the cause of the obstruction shift so that the ureter, from being quite blocked at one period, becomes patent at another, large quantities of purulent bloody urine will be passed during the patency periods; the urine in the intervals of occlusion being nearly or quite clear and natural, provided the opposite kidney be healthy.

Diagnosis.—The tumours which may be mistaken for pyonephrosis are thus enumerated by Rayer:—"On the left side of the abdomen, all those which result from morbid enlargement of the spleen; on the right side the tumours of the liver and gall-bladder; on either side the various renal tumours of another nature, such as hydronephrosis, hæmorrhage into the cavity of the pelvis, cancer of the kidney, tubercle, kidneys containing hydatid cysts; extrarenal abscess, either idiopathic or consecutive to perforation of the kidney or of the colon or cæcum; abscess arising from caries of the spinal column; tumours of the suprarenal capsules; aneurysms of the aorta; encysted tumours of different contents, hydatid or otherwise; and lastly, fæcal tumours from the accumulation of fæcal matter in the colon or cæcum."

Pyonephrosis is nearly always preceded and accompanied by febrile symptoms; the tumour is more or less painful, and the pain is increased by pressure over it, and by movements of the trunk; and when the ureter is not absolutely occluded, there is the presence in the urine of pus. In hydronephrosis there is an absence of febrile symptoms and of pus in the urine. In perinephric abscess there is even more pain than in pyonephrosis, the course of the fever is more severe and rapid, and fluctuation succeeds to ill-defined hardness about the loin and iliac region, and not to a gradually developing circumscribed tumour. In this condition there is extreme tenderness before there is any sign of fluctuation or elasticity; the thigh is often flexed upon the abdomen, and cannot be extended without much pain; there is generally redness and œdema of the skin of the loin; there is no pus in the urine; and when pus has formed in the circumrenal tissue, fluctuation is more easily made out, and is more superficial than in pyonephrosis.

Inasmuch as nephrotomy is the appropriate treatment for this last condition as well as for hydro- or pyo-nephrosis, the exact differentiation between these conditions is not so important as it would otherwise be; for when the incision is made the exact state can be made out, and the appropriate course of action adopted. It is sometimes impossible to diagnose ascending suppurative pyelonephritis with general enlargement of the kidney, from pyonephrosis. Tumour, high fever, rigors, and pus in the urine are common to both diseases.

Prognosis.—In cancer of the pelvic organs, suppuration in the vesical walls, the impaction of a calculus on one side with disease of the opposite kidney, the fatal prognosis is determined by the nature of the cause When pyonephrosis, of one side only, is produced in persons, with previously healthy kidneys, by some cause which occludes the ureter and does not interfere with the opposite kidney, the prognosis, as regards life at least, is good, if early relief to the pent-up urine and pus be given.

Treatment, in the early stages, consists in the removal, it possible, of the cause of obstruction and distension, and the improvement of the pyelitis.

If the cause be a removable or a remediable one, such as stricture of the urethra, or prostatic enlargement, attention must be addressed to that. Tumours of the ovary, uterus, and of the bladder should be removed when possible. If a calculus is felt in the vesical orifice of the ureter, it should be extracted; and in certain cases in which there are strong grounds for believing that the cause of the obstruction was a calculus impacted in the ureter, too high to be felt from the bladder and too low to be reached through the kidney, abdominal section, followed by the excision of the impacted calculus, will be justifiable and correct treatment. When the cause of the obstruction has not long existed, and is probably due to a small calculus or a plug of mucus, pus, blood, or false membrane in the ureter, it may be displaced by friction or manipulation of the tumour, if one exists, by freely drinking hot liquids, such as tea, or by active and jolting exercise, if such can be taken.

Palliative treatment of the tumour is permissible where there is not complete obstruction, and the pus and urine can escape by the ureter. In most instances, however, the proper treatment is nephrotomy, palliatives being useless, and delay dangerous. The circumstances which indicate nephrotomy are: constant pain, increasing size of the tumour, continued fever, severe gastric and intestinal disturbance from irritation or direct pressure of the tumour; inflammation of the surrounding tissues or adhesion of them to the tumour; and a threatening of rupture or ulceration of the tumour.

URETERECTOMY FOR DISEASES OF URETER

The ureter, though lying deep in the abdominal cavity, may be reached for purposes of diagnosis, or for the treatment of certain diseased states in various parts of its course, without opening the peritoneal cavity. The upper extremity of the tube, immediately below its junction with the renal pelvis, lies at the level of the lower extremity of the kidney. On the anterior abdominal wall this point may be arrived at by drawing a horizontal line at the level of the lower border of the last rib, and a vertical one at the junction of the inner and middle thirds of Poupart's ligament. The commencement of the ureter is at a point six centimetres below the point of intersection of these two lines.

It is here that a narrowing exists which has been called the upper neck of the ureter, and here the passage of a stone, that found room enough to move freely in the renal pelvis, is arrested in the first instance. This, the point of Tourneur, may be palpated in thin persons from the front of the abdomen; and in case of operation for stone can be reached by the finger inserted into the lumbar wound with the support of the other hand on the abdomen.

The ureter between this point and the entrance to the bladder is of uniform calibre; so that a stone passing the neck at the upper end is usually capable of making its way as far as the bladder, though it may be arrested by the narrow intravesical portion, or lower neck. In this part of its course the ureter lies between the peritoneum and the psoas muscle, the vessels and nerves of the pelvis being in relation with it posteriorly below, until it lies in close relation with the rectum or vagina (2½ cm. below the os uteri) before joining the bladder.

The point at which the ureter dips into the pelvis is indicated, according to Halle, by the intersection of a line joining the anterior superior spines of the ilia with one drawn vertically through the junction of the inner and middle thirds of Poupart's ligament. It is here that tenderness may be elicited in septic or tuberculous infection of the ureter; or compression may be used to arrest the flow of urine on one side, in order to collect the secretion from the opposite kidney. Should it be necessary to reach the ureter in its lower abdominal or upper pelvic part, this may be accomplished through a semilunar incision, as in the case of the ligature of the common iliac artery; the dissection being carried outside the peritoneum, which, with its contents, is pushed towards the middle line. A continuation of the incision to a point a little below the end of the last rib enables the entire upper part to be exposed. A stone impacted at the lower neck of the ureter at the commencement of the intravesical portion is within reach of the finger inserted into the rectum or vagina; and it may be removed through the bladder, after dilatation of the urethra in the female or median urethrotomy in the male, by dilating or incising the orifice of the ureter from within the cavity of the bladder.

Tuberculous or infective ureteritis may call for removal of the ureter subsequently to extirpation of the kidney; and in wounds, fistula, and hydrosis of the tube, secondary to obstruction, direct surgical treatment of the ureter may be required, either to re-establish its lumen or to provide an outlet for urine or pus, if not to remove completely the cause of obstruction, as has now been repeatedly done in impacted calculus or simple stricture.

Following the operation there may be various alterations of sensation and temporary anuria; but the ultimate issue in the cases recorded has been satisfactory.

RENAL CALCULUS

If the crystalloid substances, normally held in solution in the urine, are deposited in excess, become cemented together around a fragment of organic matter such as mucus or blood-clot, and are subsequently added to by fresh depositions from the urine, a calculus is constructed which may either be discharged with the urine, causing more or less renal colic in its transit along the ureter, or may remain behind in one of the calyces, or in the pelvis of the kidney, there to grow by fresh accretions, until it attains a size altogether in excess of anything which can pass along the ureter. Calculi may originate in the uriniferous tubes, or in one of the calyces of the kidney.

The formation of a stone in the kidney is the result of some defect in general metabolism, and is occasionally preceded by a deposit of crystals, granules, or gravelly deposit which escapes with the urine.

The tendency (hereditary in many cases) shows itself about equally in the two sexes, in childhood and after middle life. It is aggravated by a sedentary life, by insufficient fluid, and by an excess of nitrogenous or saccharine food, and possibly of the salts of lime. Renal calculus occurs with peculiar frequency in certain localities, such as in Scotland, Norfolk, Moscow, and the Delta of the Nile.

The deposition of solid matter depends, in the first instance, either upon the presence of an abnormal and insoluble product of tissue change, or of a normal product present in such excess as to be insoluble in the urine, or precipitated on account of alteration in the reaction of the fluid, which may be alkaline or excessively acid. In a great many instances the deposit is found to accrete around a foreign body or a small nucleus of organic matter; such as a mass of epithelial cells, a blood-clot, or a parasite.

The most common form of renal calculus in the adult is the uric acid, the next most common the oxalate of lime; but carbonate of lime, phosphate of lime, a mixture of phosphate and the ammonio-magnesian phosphate (the fusible calculus), cystine, xanthine, urate of ammonium, or the mixed urates, are occasionally, though rarely, found as the nuclei or chief constituents of renal stones. Alternating calculi of uric acid, oxalate of lime, and phosphates in distinct layers, are not uncommon. Renal calculi are formed at all periods of life.

The nucleus in the case of an infant is usually formed of ammonium urate; that in a person of about fifteen or sixteen years of age consists of uric acid, whilst after the fortieth year oxalate of lime constitutes the nucleus. One or many calculi may be formed in the same kidney; when composed of lime oxalate the calculus is usually but by no means invariably single.

A renal calculus may be a small, round, smooth body, or a large rough branched mass filling all the pelvis and calyces. A stone as large as a marble, sharply mammillated on its surface, may remain confined to one of the calyces for years without giving rise to more change than induration of the whole organ, due to slight or chronic interstitial inflammation. On the other hand, quite a minute stone in the tubular structure of the kidney, not much or any larger than a mustard seed or grape seed, will excite congestion, and even acute inflammation and abscess.

Renal calculi do not attain to such large dimensions, as a rule, than those which occur in the bladder. They differ much in size as well as in shape and colour, varying from that of a hemp seed to that of a small walnut; but in exceptional cases they may be very much larger. The large branched phosphatic calculi have been known to weigh as much as 1500 grains; and in one instance (Pohl, recorded by Le Dentu, p. 106) a calculus weighed even 5 lbs. They are usually rounded or oval, unless moulded to the pelvis or calyces, when they may be irregular or branched and coral-like.

The surface is usually rough or mammillated. The colour differs with the constitution of the calculus, and may vary in different layers. It is mostly purplish brown in oxalate of lime, reddish yellow in uric acid, and grayish white in phosphatic calculi, exceptional specimens being yellow, pink, green, or blue.

The liability of the kidney to calculus is equal on the two sides, and in about 15 per cent of the cases both organs are affected at once.

Pathology.—The presence of a calculus in the kidney does not necessarily provoke immediate and extensive changes in the organ. It may exist for some time at least without even exciting recognisable symptoms, especially when it is fixed in such a position as not to interfere with the function of the gland.

Atrophy of the kidney is found in some cases, chiefly post-mortem, in association with calculus; the kidney being reduced to a mere fibrous capsule around the stone. It would appear that in these cases the calculus has been loose, or so situated as to obstruct the ureter or pelvis; whence followed more or less distension of the kidney, absorption of the secreting substance, and subsequent contraction of the sac.

In other cases, where the calculus has caused obstruction of the pelvis and ureter, there ensues great distension of the kidney, beginning in the pelvis and extending to the calyces and parenchyma. Dilatation of the renal pelvis is frequently associated with interstitial œdema, and dilatation and contortion of the tubules.

The glomeruli atrophy, the cells of the connective tissue proliferate, and the vessels become thickened by the development of new muscular fibres. At the same time both the fibrous and mucous layers of the pelvis are much thickened; and it depends on the ratio between secretion with obstruction, and sclerosis, whether the kidney becomes distended into hydronephrosis or ends in contraction and atrophy. The introduction of septic organisms determines the development of suppurative nephritis, pyonephrosis, or even perinephritis; and, by inducing alkaline decomposition of the urine and secondary deposit of phosphatic salts, may lead to a very rapid increase in the size of the calculus.

Destruction of one kidney is usually associated with hypertrophy of the opposite one.

Symptoms.—A small stone may form, travel down the ureter, and escape without giving rise to any symptom; and a stone of moderate or even large size may exist for years without giving rise to any recognisable symptom. As a rule, however, there is at some time blood or albumin mixed with the urine, and some lumbar pain or aching, this may be worse at night, but is especially excited by jolting or shaking of the body, and when long continued may lead to lateral flexion of the thorax from muscular spasm.

The importance of pain about the kidneys involved, as a symptom of renal calculus, depends on its position, persistence, and direction of radiation, together with the accompanying phenomena. In addition there may be pain (so it is said, but I am sure with insufficient proof) referred to the opposite kidney or ureter, or to the bladder, with painful and frequent micturition, and at times with some pain in the testicle. If the stone have existed some time, pus, mucus, or albumin will be found daily in the urine in a minute, moderate, or considerable quantity. As soon as a stone enters the ureter, or is being propelled along it, renal colic sets in, the attack coming on suddenly, lasting a few hours, or two or three days, and suddenly subsiding to recur at some future period if the stone, instead of escaping at the lower end of the ureter, is simply displaced from the upper orifice into some less important point in the renal pelvis. Recurring attacks of colic arise also from fresh formation of renal calculus. The paroxysmal pain shoots down the course of the branches of the lumbar plexus, and is felt in the bladder, groin, or thigh, if not in all these parts; and is intensified by the spasmodic contractions of the ureter. Collapse and faintness are not uncommon; the bladder is irritable, and the urine blood-stained and loaded with urates. The attack is often ushered in with a rigor, and generally accompanied by vomiting and profuse perspiration.

When the patient is very thin, and the stone large, it may sometimes be detected on palpation of the loin. The hæmaturia is not often profuse or constant, and usually subsides with complete rest in bed; it is not proportionate to the size, number, or chemical nature of the stones, though it may be remembered that oxalic calculi have the roughest and therefore most irritating surface.

When several stones are present at one time, crepitus may be obtained. Microscopic examination of the urinary deposit may disclose casts of the urinary tubules composed of blood corpuscles, or crystalline masses which have become detached from the surface of the calculus.

Movements such as those caused by carriage exercise, running, or walking, are not in all cases needed to cause exacerbation of the lumbar pain; on merely turning in bed, or even when lying asleep, the patient may be aroused by a sudden agonising seizure.

Apart from the attacks of renal colic, lumbar and renal pain is a very common symptom of stone in the kidney. Owing to the wide nerve-connections of the kidney, the pain of renal calculus is often transferred to a distance, for instance, to the testicles along the spermatic plexus and the genito-crural nerve; to the upper part of the thigh by the same nerve, to the leg and inside of the foot by the anterior crural nerve. Paroxysmal, lumbar, and sciatic pains, accompanied or not by retching, are by no means rare. Sometimes the sciatica is severe enough to keep the sufferer within doors for weeks or months; and though the pain will be on the side of the calculous kidney, there may be nothing to indicate the cause of it. In all such cases it is prudent to institute a careful examination of the urine for blood, albumin, or crystals, and carefully to review the clinical history, especially as to any past attacks of hæmaturia.

At the same time it must be remembered that uric acid in excess and oxalic acid in the urine are often attended by hæmaturia, crystals in the urine, and wandering, transferred, and paroxysmal pains in the back, thigh, calf of leg, and sole of foot.

Prout states, and Dickinson agrees with him, that uric acid calculus produces the least pain, and that of a dull oppressive character, with a sense of weight; oxalate of lime produces an acute pain referred to a particular spot, as well as shooting to the ureter, shoulder, and epigastrium; and phosphates give rise to great and unremitting pain, attended, however, with exacerbations.

Another symptom which results from transference of nerve influence has reference to the stomach: nausea, vomiting, and dyspepsia are very common, not only at the times of actual colic, but also during the periods of less acute suffering. These symptoms are explained through the connection of the pneumogastric with the renal plexus. The retraction of the testicle, the irritability of the bladder, and the pain referred to the thorax, sometimes thought to be due to pleurisy, are all explained in the same manner as the gastric disturbance and the pains in the lower limb; namely, by transference of nerve influence.

As is the pain, so the other common symptoms of renal calculus are largely due to the actual contact of the stone with the mucous membrane of the kidney or ureter. These other symptoms are hæmaturia, pus in the urine from inflammation of the pelvis of the kidney, and the occasional sense of fulness or puffiness caused by the mechanical obstruction to the outflow of urine.

Pus is a consequence of inflammation of the mucous membrane of the pelvis and calyces of the kidney. Sometimes, as the first sign of pyelitis, before pus corpuscles are seen, the microscope reveals granular corpuscles and epithelial cells or scales mixed in fibrous threads of mucus, as well as a few blood corpuscles. Mucus occurs more frequently when the calculus is of oxalate of lime. The pus of pyelitis occurs in acid urine, is not stringy, and separates readily from the urine on standing. The urine is not offensive, except in those rare cases in which decomposition has occurred in the pelvis of the kidney, associated with considerable destruction of the parenchyma, and material affection of the patient's health.

Tenderness over the affected kidney will often be complained of by pressing on the loin or over the front surface of the organ. The peculiar attitude and gait of a patient with a renal calculus are due to an effort to relax all pressure on the kidney as much as possible. Thus, as in perinephric abscess, hydronephrosis, and other renal affections, lateral inclination of the trunk and flexion of the thigh are usual.

Among the serious complications of renal calculus may be mentioned renal colic, suppression of urine from obstruction of the ureter, hydro- and pyo-nephrosis and pyelonephritis.

Diagnosis.—Probably the greatest difficulty in diagnosis is between early strumous kidney and renal calculus. When frequency of micturition and slightly purulent urine are met with in a person of strumous habit, and are unaccompanied by a history of hæmaturia, the strumous nature of the disease is indicated; but when they are associated with a history of hæmaturia and sharp lumbar or testicular pain in an otherwise healthy-looking person, calculus is much more probable.

Lumbar pain may be due to neuralgia of the parietes or of the kidney itself; but there is not the local tenderness on examination which is met with in renal calculus.

Biliary colic is accompanied by jaundice or distension of the gall-bladder. Affections of the urinary bladder, which might be confused with renal calculus, may be cleared up with the sound or the cystoscope, or by digital examination. General diseases like locomotor ataxy, malaria, and hysteria, are sometimes accompanied by pain which might be confounded with that of renal calculus; but the other features of these diseases are characteristic of their origin.

The hæmaturia of renal calculus holds an intermediate position as regards quantity between that of malignant disease of the kidney and that due to tubercle: in the former it is extremely free, while in the latter it is little more than streaks incorporated in the mucus or pus present in the urine. Moreover, in these cases the hæmorrhage is spontaneous, and not usually associated with any increase in pain; whereas in calculus the attacks of hæmorrhage are provoked by movement or jolting, and are immediately relieved by rest, which is not observed in the other cases. Paroxysms or exacerbations of pain also are a usual accompaniment. Tumour in the lumbar region, due to distension of the kidney by obstruction, may be more rapid in formation and rate of increase, and is accompanied by more pain than the tumour due to tuberculous or malignant disease; and there may be antecedent symptoms pointing to the existence of calculus, or to calculous diathesis, before swelling begins.

When anuria occurs, the probability of its being due to calculus is great if the onset be sudden, and if pain or swelling be limited to one loin, and tenderness be discovered along the course of the corresponding ureter. This indication is strengthened by a previous history of calculus on the other side.

Treatment.—This may be prophylactic, palliative, and surgical.

(i.) Prophylaxis.—The food must be moderate in amount, and carefully selected; animal diet is to be used in moderation; an excess of nitrogenous food avoided, and diluents taken liberally.

(ii.) Palliative treatment.—Alkaline drinks or distilled water are to be used freely; and saline aperients as required. During an attack of renal colic, the hot bath, opium or belladonna fomentations, subcutaneous injections of morphia, or suppositories of belladonna and morphia are the means of relief. In very severe cases the inhalation of chloroform has been of use. Warm diluent drinks may be given, and the patient should lie with the shoulders and thighs raised.

(iii.) Surgical treatment.—When the symptoms of stone are severe, and are not removed or rendered bearable by several months of medicinal treatment and rest; when, in order to diminish pain or hæmaturia, the patient is compelled to confine himself to the recumbent posture; or when anuria supervenes upon the symptoms of calculus in one or both kidneys, *nephrolithotomy* is indicated. The object of this operation is to save the kidney. If, however, the organ is in great part destroyed, if there is calculous pyelitis, or calculous hydronephrosis or pyonephrosis, *nephrotomy* and extraction of the stone are the necessary measures.

If, after the kidney and ureter have been thoroughly explored—not only over the outer surface, but by digital examination of the interior of the renal cavity—a stone cannot be detected, and yet the symptoms point definitely to the presence of stone, and the patient's life is insufferable from pain or hæmorrhage, *nephrectomy* is the last resource.

In infants Dr. R. A. Gibbons has described the effects of uric acid concretions in their passage down the ureter. The testicle is drawn up, there is evidence of great pain and tenderness on the corresponding side of the abdomen; the urine is clear, scanty, and passed frequently in small quantities with considerable pain, accompanied by minute cayenne-pepper-like grains of uric acid, and sometimes a little blood. This condition is the cause of more or less incontinence of urine, the child frequently wetting itself, both by night and day.

True calculi, according to Henoch, are as common in children as in adults; but in their passage down the ureter the child suffers much less pain than the adult. The stone is composed of uric acid, and the subjects of stone are always the offspring of gouty parents, and for the most part are males. The attacks of renal colic occur with remarkable suddenness, and without any premonitory signs of illness.

In treating these cases hot baths are to be employed, followed by poultices or fomentations to the loin on the affected side, and the administration of a mixture containing bromide of ammonium, sal volatile, and compound tincture of camphor. In older children it has been found that a mixed ordinary diet combined with tonics and an abundance of fresh air afford the most effective means of combating the defective metabolism which results in the excessive formation, and separation, of uric acids and urates.

MORBID GROWTHS

The kidney is liable to many morbid growths of a cystic and solid character, both benign and malignant. Several of these do not attain to any great size, or cause the kidney to become appreciably if at all enlarged. Thus *adenoma*, which occurs in two forms in the kidney (the papillary and the alveolar), is usually the size of a hazel-nut or walnut, and seldom, if ever, so large as an egg or small orange; *angeiomata cavernosa*, though distinct formations, or new growths of reticulated cavernous tissue, are of quite small size, not exceeding that of a marble, and, though called tumours, the parts which they affect are often shrunken, rather than projecting or enlarged; *leukæmic tumours* are small, scattered, roundish patches of lymph-cells following the course of the capillary vessels, and looking not unlike extravasated white blood-cells, though they are sometimes actively growing tumours of a truly malignant character; *lymphadenoma* is found in the kidney, associated with similar disease of the glands, liver, and intestine; *fibroma* occurs "in the form of small white knots of fibrous tissue near the bases of the pyramids" (Moxon), but occasionally a very large simple fibrous tumour has been found in the kidney; *syphilitic gummata* occur occasionally, but do not attain such a bulk as greatly to increase the dimensions of the kidney; various-sized and numerous cysts, as in granular kidney, may be present without adding to the size of the organ.

Though pathologically of the nature of "tumours," yet, clinically speaking, some of the above-mentioned formations never give rise to actual tumours; others do so but rarely.

Clinically, any enlargement of the kidney, which can be detected by physical examination at the bedside, is spoken of as a tumour of the kidney. Some of these enlargements have been considered already, namely, hydronephrosis, pyonephrosis, renal abscess, and the enlargement of the kidney caused by scrofulous disease.

I may here mention, incidentally, that the comparatively rare condition brought about by hæmorrhage within the capsule of the kidney is liable to be mistaken for tumour or other renal enlargement, or for calculous disease of the kidney. Subcapsular hæmorrhage may result either from direct traumatism or indirect strain; the quantity of blood effused varies from a few drachms to a pint or more. The symptoms produced are local pain, tenderness or discomfort, and undue frequency of micturition. They are in fact very similar to those resulting from the presence of a renal calculus, with or without the hæmaturia; and in those cases where the blood effusion is large it is not at all unlikely, by its bulk and renal contour together with the hardness and nodulation which result from coagulation, to simulate a renal tumour very closely.

The subsequent effect of organisation and contraction of the clot is to compress the organ and seriously to impair its function, so that early relief by operation is of importance; and the difficulty of distinguishing between it and calculous pyonephrosis or other form of tumour, except by exploration, becomes of less moment. The history of the affection may be a guide in some instances, the symptoms occurring suddenly, and dating from a blow or wrench. Such an accident, however, so readily calls attention in the first instance to a tumour, or causes sudden pain and enlargement by hæmorrhage from a previously existing new growth, that too much reliance must not be placed upon it.

Malignant disease of the kidney.—*Pathology.*—Malignant tumours of the kidney include several different forms of new growth. The larger number are sarcomata, which appear at the extremes of life. Of 67 cases of malignant disease collected by Sir William Roberts, 25 occurred in children under ten years, 3 only of these after five. These infantile tumours are almost invariably sarcomatous, and are remarkable for the rapidity of their growth and the enormous size to which they attain: Sir Spencer Wells recorded that a tumour removed from a child of four weighed nearly 17 lbs., and others have been found exceeding 30 lbs. in weight. Sometimes both organs are invaded at the same time. Of 67 instances quoted above, 60 were unilateral, and in 3 only was it clear that the disease was primary on both sides. According to Guillet, from observations chiefly made after death, only 7 out of 72 cases were bilateral. In 1880 Dr. Abercrombie exhibited three cases at the Pathological Society in which both kidneys in children were invaded from the hilum by sarcoma. The incidence of malignant disease appears to be pretty equally distributed on the two sides; but as regards the influence of sex there is a remarkable preponderance in favour of males; the proportion being as 47 to 19 (64 to 35, according to Guillet). This disproportion in distribution is not so well marked in the case of children; the proportion of males to females being as 15 to 9 in those affected up to ten years of age.

In children, growth is extremely rapid, metastasis occurs early, and death usually results within a year. The distribution of the secondary growths takes place with nearly equal frequency in the lymphatic glands, the lungs, and liver.

Sarcoma supplies by far the greatest number of malignant tumours, it occurs either before the age of five, in which case the disease may be bilateral, or at any subsequent age when they are unilateral and of somewhat slower growth.

In infancy, sarcomata are usually encapsuled, and for the most part, in causing enlargement, do not alter the shape of the gland. Their growth is very rapid and the size attained enormous. The glandular substance of the kidney is almost completely destroyed. These tumours are composed either of round or spindle cells with groups of tubules between; and in most cases there are present also large fusiform cells with cross striation, having under the microscope the appearance of muscle fibre. The enlargement is painless, hæmaturia is rare, and secondary nodules form early in other organs. Removal of the tumour is not to be recommended, as young children do not bear interference with the viscera well, and those who have survived the operation have died from recurrence or other mishap within a year.

Sarcoma in adults is for the most part composed of fusiform cells, and from the admixture of large striated fibres in bundles is in some instances called myosarcoma. One side only is attacked; hæmaturia occurs frequently, and large quantities of blood are lost at a time. The tumour rapidly attains a large size and is accompanied by considerable pain, while secondary deposits occur in other organs. The results of operation have until recently not been very much better than in children, death commonly occurring within a year of nephrectomy. This has nevertheless been performed in many instances on account of the pain and inconvenience of the swelling.

In a recent series of five cases, reported by Dr. James Israel of Berlin, there were three complete recoveries in female patients aged respectively fourteen, forty-three, and six years; the tumours being alveolar sarcoma, myxosarcoma, and spindle-celled sarcoma respectively: while two males, aged five and fifty-one, from whom round-celled and cysto-sarcomata were removed, died of recurrence and metastasis within a few months.

Other allied forms—such as *melanotic sarcoma*, in which melanuria occurs; *myxosarcoma*, in which the tumour is soft and jelly-like and of very rapid growth; and *lymphosarcoma*, which is scarcely ever limited to the kidney—are all extremely rare.

Carcinoma for the most part affects the kidney in the encephaloid form. It arises in the cortex and invades the rest of the organ, usually beginning at one pole; the growth is of the consistence of normal brain substance, pale, not very vascular, and generally encapsuled. The mass is seldom quite uniform, being occupied by areas of liquefaction, of colloid degeneration, or extensive hæmorrhages; and in rare instances by induration of the nature of scirrhus.

Carcinoma attacks the kidney twice as often in men as in women, and usually in the latter half of life, nearly all the cases occurring after forty-five. Cancer has a more protracted course in the kidney than it generally runs in other abdominal organs, lasting in some cases four or five years or even longer, and resulting in a tumour of enormous size, weighing 15 to 20 or more lbs. In the Middlesex Hospital Museum there is a cancerous tumour weighing 31 lbs. from the left kidney of a boy aged eight years.

The symptoms are hæmaturia, often copious and most marked in the early stage; the appearance of a tumour in the lumbar region, which grows steadily; and the occurrence of aching and neuralgic pains or of a sense of weight in the side. Varicocele is present sometimes on the left side as a remote sign due to obstruction of the spermatic vein; and the wasting, anæmia, and loss of strength common to cancer in other parts are present here, nor is evidence of secondary deposits wanting, at all events in the later stages.

As regards treatment, most of the cases offer no hope of cure, the disease not being discovered till too far advanced for eradication. In cases which are diagnosed early, before secondary infection has occurred, nephrectomy may be performed with some hope of cure. Dr. James Israel, in 1894, reported six cases so treated, of which three ended in recovery.

Epithelioma is met with in rare instances. The cells of which the growth is composed are more often cylindrically arranged, and are columnar in shape, with rounded free extremities and a clear protoplasm. Both the cells and their arrangement resemble very closely what obtains in the convoluted tubes, even to the maintenance of a central lumen; and this is accurately repeated in the secondary deposits.

Instances are upon record of squamous epithelioma attacking the kidney primarily. In a case published by Robin, and quoted by Roberts, the cells resembled the pavement variety, and were remarkable for their size, measuring $\frac{1}{10}$th of a millimetre in length. No nests were found as in an ordinary cutaneous epithelioma.

In another case, recorded in the Middlesex Hospital Report for 1892, the tumour of the left kidney weighed 28 lbs., the bulk being due largely to calculous pyonephrosis; there was in addition soft new growth arising in the pelvis of the kidney, and secondary deposits in the lungs, liver, and retroperitoneal glands, all of which possessed the microscopical features of squamous epithelioma. The patient was an old woman of eighty-two. In this case the origin of the new growth appears comparable to that arising in the gall-bladder in connection with gall-stones.

Benign tumours.—*Myxoma* sometimes attacks the kidney and rapidly develops into a large soft tumour. A case of this sort, occurring in a man of thirty-nine, causing death within a year from the first discovery of the tumour, without metastasis or hæmaturia, and with symptoms only of pressure and wasting with some abdominal pain, is recorded in the Middlesex Hospital Report for 1895.

Villous papilloma is found in the renal pelvis in rare instances. Like this disease in the bladder, it causes severe hæmaturia sometimes accompanied by fragments of detached villi. Enlargement of the kidney is not marked, but, as in other cases of renal hæmorrhage, there may be casts of the ureter to indicate its source.

Adrenal tumours and Accessory adrenal tumours, which have a superficial resemblance to sarcoma and are frequently mistaken for it, arise in the suprarenal body, or in disconnected portions lying either free in the immediate vicinity or embedded in the cortex of the kidney beneath its capsule. They contain fat, and have been described as renal lipoma; but when the fat is removed by solution in ether, the identity of the structure with that of the fascicula reticulosa of the suprarenal is evident enough, and from analogy with similar developments in connection with the thyroid gland. Virchow has proposed for these tumours the term "struma suprarenalis," and the accessory forms are referred to in modern German literature as malignant struma of the kidney. When either the entire gland or one of these included portions takes on rapid growth, a tumour is formed which, both on account of its size and tendency to metastatic development, becomes dangerous to health and life.

An excellent example of this uncommon form of tumour was removed by me from a man aged forty-three. Many unsuspected secondary nodules were observed in the liver during the operation, and there was also a hard nodule attached to the temporal region of the skull. The case was published in the first volume of the *British Medical Journal* for 1893; and I there drew attention to the analogy of this form of tumour to the rare variety of goitre, associated with secondary deposits structurally identical with the thyroid gland in the bones and viscera; I published an instance of this kind in the *Transactions of the Pathological Society*, vol. xxxi.

Diagnosis and Treatment of renal tumours.—The recognition of adrenal or accessory adrenal tumours as solid growths of the kidney is not, as a rule, a matter of difficulty; but to distinguish between them and other renal tumours without microscopic examination is at present impossible. Adrenal growths, however, do not run so rapidly fatal a course as sarcomata; they are not bilateral like some of the congenital or infantile forms of the latter disease, and when affecting the suprarenal body itself do not cause hæmaturia. These tumours may be removed with a fair prospect of cure, and a successful case is recorded by Dr. James Israel in a man of forty-two who was reported well a year after the operation.

Malignant growths of the kidney are for the most part rounded, smooth, or lobulated, and without the sharp edge possessed by the spleen or liver; in the infiltrating forms the tumour retains something of the original shape of the kidney, though no trace of the glandular substance may remain. With the exception of the comparatively rare cases in which the kidney is invaded by sarcomatous growth from the hilum, the new development almost invariably begins in the cortex and spreads thence to the pyramids; sometimes it invades the pelvis, ureter, or renal vein, or even the vena cava. In this way, or by pressure on or infiltration of the walls of the vena cava, or aorta, obstruction is caused which may lead to œdema or gangrene of the lower extremities, or to effusion into the peritoneal cavity.

As a general rule the tumour is contained within the proper capsule of the kidney, which may be thickened and covered with dilated veins, or may be continued by fibrous tracts and dissepiments into the substance of the new growth, rendering attempts at intracapsular enucleation dangerous or impossible. In exceptional cases the capsule is perforated, and neighbouring organs, or the parietes, are infected by continuity. The consistence of the mass is affected by caseous, fatty, or colloid degeneration of its substance, or by extensive hæmorrhagic effusion.

Tumours of the kidney occupy a characteristic position deep in either lumbar region, for the most part high up within the cavity of the abdomen; but when small and non-adherent, they descend with inspiration: when large, they extend towards the pelvis and across the middle line of the abdomen. There is often some bulging in the loin, and in any case the mass should be more easily felt from behind, and should play freely between the hands placed over the abdomen and the loin. The descent of a renal tumour on inspiration, though distinct enough to distinguish it from a swelling of pelvic origin, is very much more limited than in the case of the liver, spleen, or stomach, or growths connected with them; and lateral movement is practically not permitted at all. The intestines lie towards the centre of the abdomen, the tumour being close up to the flank, with the colon in front; and, if the mass be not too large, there is an area of resonance above and below it, separating it from the liver above, and continuous with the resonance in the hypogastrium below.

Very large tumours on the left side may displace the spleen and stomach towards or beyond the middle line; and on the right side may reach the diaphragm, displacing and tilting the liver, so that its edge occupies a vertical instead of a horizontal position near the middle line of the abdomen.

In the majority of cases the growth begins at one or other extremity of the kidney, more often at the upper. The mass formed is then definitely encapsuled; and when small and situated deep under the margin of the thorax is very difficult to make out. But as these are the cases which are most favourable for operative treatment, the tumour and kidney being usually readily separated and unattended, in the early stage at least, by secondary growths, it is of the utmost importance to diagnose them early. Their presence is indicated, before the recognition of a tumour, by hæmaturia, often very profuse and coming on independently of shock or exertion; and by pain, tenderness, or discomfort in one or other loin. With the aid of a thorough examination, under an anæsthetic if necessary, even a small swelling can be made out through thin abdominal walls; and this, together with the other symptoms, is sufficient to warrant an exploratory incision which may finally show the necessity for removal of the kidney. This opinion has been illustrated by two cases diagnosed and operated upon by Dr. James Israel of Berlin (the growth being no larger than a cherry in one instance), both of which ended in complete recovery: the patients reported themselves three years after operation.

CYSTS OF THE KIDNEY

Simple or serous cysts, which are met with for the most part in the kidneys of elderly people, may attain considerable size, and so constitute a troublesome disease. They cause no symptoms except those due to their size and to the pressure they exert on surrounding organs.

These simple cysts arise in the cortex of the organ, and project in relief from its surface, the rest of the kidney being healthy and functionally active; or it may be granular, or more or less atrophied from the pressure of the cyst itself. Sometimes a communication is established between the cyst and one of the calyces of the kidney.

The contents of the cyst are fluid, containing a small quantity of albumin and a little saline matter; but rarely, if ever, any urinary ingredients. Occasionally they contain blood from the rupture of blood-vessels in their walls, and sometimes a jelly-like or colloid material.

Their exact mode of origin is uncertain.

Symptoms. — Simple renal cysts begin insidiously, grow slowly, present themselves first in the loin, or in the lumbar area of the front of the belly, and may be so hard at first as to be mistaken for solid growths. As they increase, they gradually encroach upon the greater part of the abdominal cavity; their point of attachment ceases to be even approximately ascertainable; and in woman they may give rise to the suspicion of ovarian tumour. As they grow they tend to spread out the renal substance, so that a good part of the kidney may be stretched in a thin layer over the attached part of the cyst wall.

Diagnosis.—The difficulties which surround the diagnosis of these very rare cysts are extremely great; for not only may they be mistaken for hydatid of the kidney, hydronephrosis, and other renal tumours and perinephric fluid collections, but it may also be almost impossible to distinguish them from solid tumours in the parietes, from hepatic or splenic cysts, or cysts of the omentum, mesentery or pancreas, from malignant cystic tumours springing from the pelvis or elsewhere within the belly, and, sometimes in women, from ovarian cysts.

Treatment.—When they become so large as to be inconvenient they should be tapped; if they refill, they should be laid open and the edges of the cyst stitched to those of the wound: the cyst will then collapse, and probably close. Smaller cysts should be excised from the kidney.

General cystic degeneration of the adult kidney.—This is the result of a degenerative process. The whole kidney is converted into a vast number of conglomerated cysts of varying size, which leave scarcely any portion of the glandular structure unchanged, and give a greatly increased bulk to the organ, which, while retaining the renal shape, may be ten times the bulk of the normal kidney.

The cortical and medullary portions are alike replaced by the cysts which bulge the capsule and protrude on the surface as translucent sacs. The cysts vary in size from microscopic dimensions to that of a grape or walnut; the largest being often in the centre of the organ.

The fluids contained are clear, pale straw-coloured, dark yellow, purplish, or deeply blood-stained. In consistence these contents are limpid, serous, viscid, colloid; or turbid, caseous, and almost solid. Occasionally they are purulent; sometimes even solid, in which case they consist of molecules of fat, epithelium, and crystals of cholesterin, uric acid, or triple phosphates. The cysts do not communicate with the pelvis, or calyces, nor with each other. They are closed cavities, whose walls are excessively thin, and lined by a delicate layer of epithelium. They probably owe their origin to expansion of parts of the uriniferous tubules and atrophy of the interstitial tissue. The original renal substance is in some places wholly removed, in other places small portions between the cysts remain unchanged.

Sometimes the renal pelvis, but not the ureter, is much dilated. The dilatation is due, not to obstruction, but to dragging. In one of my cases the pelvis was enormously dilated. Both kidneys are commonly affected. Dr. Dickinson found only one case out of twenty-six in which the disease was confined to one kidney. A patient from whom I removed a kidney of this kind nearly four years ago is still alive and well.

"Congeries of Renal Cysts" are sometimes congenital, and lead to enormous abdominal distension of the fœtus in utero, with serious difficulty in parturition. Cystic degeneration is a cause of death of the fœtus in utero or during birth; and it is sometimes found associated with various malformations, such as talipes, cleft palate, and imperforate anus The observations of Naunyn led him to regard the condition as one of adenoma. Courbis would prefer to call the condition epithelioma, but for the meaning usually associated with that word. "In the early stages the cyst walls have a membrana propria, and are lined with tesselated epithelium, which in advanced specimens is difficult of detection. When the disease is not far advanced, the renal pelvis is easily recognised; but in the later stages it becomes filled with fatty tissue." The ureter is narrow and the vessels are small. "Minor degrees of the affection are not incompatible with life, and several instances are known in which such kidneys have been found in adult individuals." Mr. Shattock has advanced the opinion that in these kidneys there is a combination of mesonephros (Wolffian body) with the metanephros (true kidney); and that the cysts may be regarded as arising in remnants of the mesonephros embedded in the true kidney. It cannot be said that there is nothing to support the view that the condition depends on obstruction of the urinary passages, though in the fœtus as in adults obstruction in the ureter leads to dilatation of the kidney, but of the nature of hydronephrosis.

Symptoms.—The clinical history of this disease, according to Wilks and Moxon, is much the same as that of Bright's disease, "of which, notwithstanding their vastly different appearance, these enormous-looking tumours form only a variety. The cysts are, in short, an excessive production of that minuter cystic condition of the kidney which we have already described as occurring in granular kidneys." As with granular kidneys, so with the large cystic kidney, hypertrophy of the heart is not infrequently associated. In one of my cases the left ventricle was much hypertrophied, the right kidney was converted into a congeries of cysts, the secreting structure almost gone, and the pelvis enormously dilated; the left kidney was large and granular, had a wasted cortex, and was puckered in places on the surface.

The subjects of the large cystic kidney (not congenital) are more often men than women; and are always adults, the majority being persons at or past middle age. In six cases the ages of the patients were thirty-nine, fifty, sixty-five, two between thirty and forty, and one twenty-one years respectively. Out of 21 cases mentioned by Dickinson, the ages of 11 were between forty and forty-nine. In this form of disease there is no tendency to dropsical effusions; but pain in the loins and hæmaturia, especially the latter, are frequent and pronounced symptoms, and are useful in diagnosis.

When œdema occurs in a case of cystic kidney, it is the mechanical effect of pressure of the tumour. The characters of the urine are like those of the granular kidney. It is pale in colour, abundant in quantity, of low specific gravity, and albuminous even when not admixed with blood.

Coagula and granular casts are occasionally found in the urine, and more rarely pus in small amount.

However, the symptoms are not always very obvious.

In one case, the specimen of which is in the Hunterian Museum, the patient at sixty-seven died of apoplexy; his vessels were atheromatous, and his heart weighed only 9½ ounces. Both kidneys were enlarged and cystic; their state had not been recognised during life.

In another case, the patient, a sailor aged fifty, presented symptoms of brain disease, became delirious, and died in a few days. Both kidneys were almost entirely converted into congeries of cysts.

In a third case, a shoemaker had severe pain in the loins and along the course of the ureters for five years; his urine was scanty, and always mixed with blood or pus. The other symptoms were numbness of the right leg, frequent severe headache, and occasional œdema of the lower limbs. Both kidneys were large and cystic, and the ureters were dilated.

Diagnosis.—When, with a sallow complexion, hypertrophy of the heart, and increased arterial pressure, are found the above characters of the urine and a tumour in each of the renal regions, or a tumour in one and an increased fulness in the other, the diagnosis of "large cystic kidney" is pretty clearly indicated.

The tumour will probably be yielding; but it does not fluctuate, and it presents the usual topographical characters of renal tumours in general.

In the late stages of the disease, obstinate vomiting, convulsions, suppression of urine and coma supervene, and then follows death.

Death sometimes occurs from exhaustion brought on by hæmaturia; sometimes from bronchitis or pneumonia; sometimes from œdema of the lungs, and sometimes from some quite independent cause. Of the three fatal cases in my list, one died of bronchitis, congestion of the lungs, and morbus cordis; one of epithelioma of the tonsil and soft palate; and the third of epithelioma of the penis.

When death is caused immediately by the state of the kidneys, the manner of death is most frequently by uræmia. The progress of the disease is not usually very rapid, from two to five years being a common period.

Treatment.—This should be based upon the same principles as that of interstitial nephritis. Moderate stimulation of the skin and bowels, with the avoidance of excess of nitrogenous food or exposure to unnecessary cold or exertion, so as to keep the production of nitrogenous waste down to the lowest point while promoting elimination vicariously, constitute the best general methods. As regards drugs, a laxative mixture containing iron is the most efficacious; and if the heart show signs of feebleness, strychnine and digitalis may be added with advantage.

The surgeon's aid will not often avail, owing to the frequency of the bilateral incidence of the disease; and when unilateral, unless the size be very inconvenient, no surgical treatment is called for. However, in two out of three cases in which I have removed such kidneys the patients have recovered.

Paranephric cysts are neither developed in the kidneys nor are they due to a dilatation of the renal cavity or pelvis. They encroach upon the surface of the kidney from without, and if they have any communication with the interior of the organ, it is only secondary and due to a fistulous passage formed between the cyst and the kidney.

Such cases must be treated like hydatid, simple cysts, and hydronephrosis; namely, they should be opened and drained, the edges of the cyst being stitched to those of the wound in the abdominal parietes: or they should be entirely excised.

HYDATIDS OF THE KIDNEY

Hydatid cysts form tumours in connection with the kidney. The kidney stands third in order amongst the viscera favoured by this parasite, being thus more frequently affected than any other organ or tissue of the body except the liver and lungs.

The left kidney seems to be affected nearly twice as frequently as the right; owing perhaps to the shortness and directness of its arterial branch. The cyst may be immediately beneath the capsule, or lodged deeply in the substance of the kidney. In either case, as it grows it forms an elastic, rounded, and sometimes fluctuating tumour projecting from the surface of the organ. The whole kidney may ultimately be destroyed by the cyst, which may come to fill a large part of the abdominal cavity, but in the majority of cases it remains quite small, and does not exceed the size of an egg or an orange, because the contents of the cysts find an escape by the ureter.

A renal hydatid cyst may burst into the pelvis of the kidney or into the intestine or lung. Sir William Roberts tells us that it has a natural tendency to discharge its contents by the ureter; and out of 63 cases collected by him, hydatids were discharged by the ureter in 52: in 47 the cysts opened into the pelvis of the kidney only; in 1 into the pelvis of the kidney and the lung; in 3 into the intestine; and in 1 into the stomach, as well as into the renal pelvis. In 1 case the opening was into the lung only; in 2 the cyst was opened artificially, and in 8 cases it did not open at all. Roberts states that there is no authenticated case of a hydatid cyst of the kidney opening in the loin, and that Rayer's two cases which so opened were hydatids in the muscular tissue of the lumbar region. In a third case there was post-mortem proof that the cyst was unconnected with the kidney.

Symptoms.—In some instances there are no symptoms, and the cyst is met with as a post-mortem surprise. In others there are no symptoms until the cyst bursts, after the common manner of the disease, into the renal pelvis, when attacks of renal colic begin and recur from the passage of the daughter cysts and portions of the hydatid membrane along the ureter. In a third class of cases there is an abdominal tumour, with or without the symptoms excited by the escape of the contents of the cyst along the urinary passages.

In 18 out of 63 cases, according to Roberts, a tumour in the side was discernible during life, and varied in size from an orange to an adult head. Fluctuation is not always to be detected, either because of the extreme tension of the cyst walls, or because of the small proportion of fluid to daughter and grand-daughter cysts. The hydatid thrill or fremitus has been seldom observed. The hydatids discharged by the urethra are in various states; broken or entire, as fragments, or as vesicles simply collapsed. There may be one or two only, or scores of vesicles. Some contain only water, others have minute cysts within. Crystals of uric acid have been found adhering to them; crystals of triple phosphates, uric acid, and oxalate of lime have been found within. When the parent cyst has suppurated before bursting, pus is discharged as well as hydatids. Blood is sometimes discharged in the urine. In a case of which I have notes, the cysts were mixed with large quantities of pus in the urine, but some of the smaller and unruptured cysts contained the ordinary clear saline and non-albuminous fluid characteristic of hydatids. In some cases, hooklets, shreds of hydatid membrane, and oil particles, but no vesicles, are found in the urine.

In relation to the discharge of hydatids by the urethra, it must not be forgotten that hydatid cysts of the liver have sometimes discharged into the renal pelvis; and hydatids in the cellular tissue of the pelvis, or in the track of the ureter, have broken into the bladder or ureter, and thus escaped by the urethra.

Such cases are infinitely rare. Mr. Birkett knew of one case in which hydatids were withdrawn by a catheter from the bladder, the cysts having escaped into the bladder from a hydatid tumour between it and the rectum. Other similar cases of hydatid tumours in this situation opening into the bladder are on record; but they are to be distinguished from hydatids in the kidney by the formation of a pelvic tumour, and by the prolonged and increasing pressure-effects upon the bladder and rectum.

The escape of the vesicles may or may not excite nephritic colic. There may be one or several discharges at longer or shorter intervals of a few months or several years. Sometimes at the first escape the cyst empties itself and dries up, in other cases there have been numerous periods of escape over many years, and at uncertain and very variable intervals.

Pain in the lumbar region and along the course of the ureter of the affected organ, with a sensation of something giving way, usually precedes the discharge. Rigors, vomiting, spasmodic colicky pains, and sometimes suppression of urine and retraction of the testicle, accompany the passage of the vesicles along the ureter, which takes from a few hours to several days to be accomplished; then comes a period of relief during their stay in the bladder, and this is followed by the distress, retention, and painful efforts to micturate which indicate their journey through the urethra. An accident, such as a blow, kick, or fall, or the jolting of horseback or carriage exercise, may lead to the rupture of the tumour, and to the first or to any subsequent escape of the vesicles.

When a tumour exists, and is very large, it may fill the loin, and to a greater or less degree the corresponding side of the abdomen. It may be quite round and regular in outline, or present a somewhat nodulated surface. Its relations to the bowel and to the ribs and surface are the same, and are subjected to the same exceptions as renal tumours generally.

In a case shown by Dr. Fotheringham to the Glasgow Pathological Society (11*a*) the patient had a nodulated tumour, which filled the right lumbar region, and caused pain and tenderness; the ordinary symptoms of Bright's disease were also present. Within a fortnight, after suppurating and discharging pus and cysts by the urethra, the symptoms of Bright's disease disappeared.

Suppuration may occur as the result of violence or of puncture, whether for the purpose of diagnosis or treatment, or independently of either. If it occur, then rigors, fever, and increased pain and tension about the tumour set in.

Prognosis.—The prognosis of renal hydatids is not always unfavourable. Sir W. Roberts' list of 63 cases yields 20 in which recovery was believed to have been permanent, and 19 of which were fatal; in the remainder (24) the results were not known. In 10 of the fatal cases the cause of death was directly due to the hydatids bursting into bronchi, to pleurisy, to the effects of pressure of the tumour, or to suppuration of the contents. In one case a large renal calculus was found with the hydatids in a solitary kidney, and the hydatid tumour opened into the renal pelvis, and thus obstructed the outflow of urine. In 9 cases the causes of death were unconnected with the hydatids.

The duration of the disease is uncertain, but often very much prolonged. Patients have gone on passing vesicles at intervals for twenty and even thirty years. There are no means, except by waiting, of telling whether more remain behind after some have escaped by the passages. If, when the cases are left untreated, the prognosis of hydatid tumours of the kidney is more favourable than that of similar tumours of other internal organs, it is because of the tendency to rupture into the renal pelvis. When the tumour is small, and situated in the central parts of the kidney, the evacuation is easy and safe. There is no fatal case on record when the vesicles have escaped by the urethra from a renal hydatid cyst which had not given rise to an abdominal tumour. The discharge of pus with the vesicles is not necessarily unfavourable; patients have recovered when the quantities of pus discharged have been very great. When the cyst breaks into the pleura or bronchi the probability of recovery is not good; when into the bowel or stomach it is much more favourable. When the cyst grows continually, and does not burst in any direction, the dangers of a large tumour and of its pressure-effects have to be met.

Diagnosis is made certain when, with a tumour in the renal region, there is a discharge by the urethra of hydatid vesicles or of the other products of hydatid tumour. If the cyst do not rupture into the renal pelvis the urine will present no evidence of the nature of the disease; and if a tumour exists without discharging its contents by the ureter there is nothing to point out the precise nature of the enlargement except the use of the aspiratory trochar. The renal origin of the swelling must be diagnosed by the same means as other renal tumours. When vesicles are voided but no tumour exists, nephritic colic generally indicates the locality of the hydatids.

Treatment.—When a tumour increases without discharging by the urethra the only proper treatment is to cut down upon the tumour, and having tapped and emptied it of its fluid contents, to incise it and stitch the edges of the cyst to the margins of the parietal wound. The cyst should be opened from the loin if possible; if not, then at its most prominent or projecting point. When the kidney is very extensively affected, nephrectomy will be necessary. When there is no tumour, and hydatids are discharged by the urethra, no surgical treatment is absolutely needed unless renal colic is frequent and severe; but in my opinion it is distinctly better to explore the kidney and excise the cyst. [Cf. vol. ii. p. 1140.]

DIAGNOSIS OF RENAL FROM OTHER TUMOURS

Renal tumours are among the most difficult of abdominal enlargements to diagnose correctly. The chief distinctive points about them are the following:—

1. The large intestine is in front of the tumour. Normally the right kidney, unless enlarged, lies a little way from the lateral wall of the abdomen, behind and to the inner side of the ascending colon; not in close contact with the abdominal wall, and outside the ascending colon, as the liver does. When enlarged, the ascending colon is usually placed in front of the tumour and towards the inner side of it. On the left side the descending colon is in front of the kidney, and inclines towards its outer side below; in some cases coils of small intestine may overlie either right or left tumour, if the enlargement be not sufficient to bring the kidney into direct contact with the front abdominal wall. When the colon is empty or non-resonant, it can be felt as a roll on the front surface of the tumour, and the anterior walls can be felt to travel over the posterior as oblique pressure is made upon the gut.

[illegible] a splenic tumour, and, but [illegible] Rarely, if ascites is present, [illegible] and misshapen manner, the small [illegible] liver and the abdominal parietes.

As an exception, a right renal tumour may push the ascending colon down instead of bearing the gut forwards in front of itself. A tumour of either kidney may push the bowel to its inner side towards or even beyond the median line, in which case there is no resonance in front of the tumour (15a).

2. There is no line of resonance between the kidney dulness and the vertebral spines, and no space between the kidney and the spinal groove into which the fingers can be dipped with but little resistance, as there is between the spleen and the spine.

3. Renal tumours do not project or protrude backwards to any marked extent. They fill up the hollow of the loin, and may even cause some actual fulness there; but often there is nothing more than the effacement of the natural hollow of the loin. When the tumour attains a large size the parietes may be projected laterally to a degree sufficient to be observed by a superficial glance. Sir William Jenner says: "Renal tumours never cause enlargement behind. A renal tumour is not visible in the back, it expands in front. A little greater fulness of the loin there may be, but nothing like tumour. . . . Tumours due to disease of the kidney enlarge in front; whilst abscesses and other lesions which may simulate renal tumours often cause considerable posterior projection." A renal tumour may, however, as quite an exceptional thing, cause pointing on the posterior aspect of the body. Mr. Holmes reports a case of pulsating cancer of the left kidney presenting a swelling over the sacrum, and causing œdema of the back as high as the neck.

4. "The kidney has no sharp edges. It is rounded on every side, and in disease never loses this peculiarity" (Jenner). Whether solid or cystic, and of whatever size, a kidney tumour is prone to retain some, often much, of its natural outline.

When the tumour involves only a part of the organ, and not the whole, and therefore does not expand the entire capsule as it grows, it is unusual for it to have the renal outline.

5. Renal less frequently and less markedly than hepatic, splenic, and suprarenal capsular swellings descend in inspiration. Hepatic and splenic enlargements, and more especially the latter, are depressed by the contraction of the diaphragm, whereas kidney swellings are often quite fixed in their position. If the kidney and circumrenal tissues have been inflamed, the kidney will be bound down in its natural situation, and [illegible] but in cases of new growth, where the organ [illegible] there may be a [illegible]

[illegible] ought [illegible] symptoms.

6. As a rule, renal enlargements [illegible] the median line, and frequently are separated from the [illegible] by a resonant area.

Either a cystic or solid renal tumour may ultimately attain such a size as to occupy the greater part of the abdomen. Numerous instances of this kind are recorded; but they attract attention long before this stage is reached, and while they are still limited to one side of the abdomen.

7. When the tumour is large enough to reach the front wall of the abdomen, the most anterior point at which it comes in contact with the parietes is commonly about the level of the umbilicus, or a little higher; the lateral wall between the costal margin and the crest of the ilium is then also bulged outwards.

When malignant growth or abscess affects only part of the kidney, the abdominal tumour may appear to be somewhat removed from the strict limits of the renal region. Thus, when the upper part of the kidney is alone involved, there is much upward bulging, and the tumour may be felt in the part usually occupied by liver or spleen. In malignant disease of the right kidney I have seen the tumour occupy a great part of the right hypochondriac region, and simulate a hepatic tumour.

8. There is a symptom which occurs in large tumours of the left kidney, and not in splenic enlargements, namely, varicocele of the left side, which gradually increases with the growth of the tumour. In one case I operated upon, the varicocele was very large, and the spermatic vein with the inferior mesenteric vein curved over the front and inner side of the tumour, and was enlarged to the size of the ring-finger.

Little or no reliance can be placed on the absence of changes in the urine. Solid tumours do not always cause hæmaturia, nor do accumulations of pus in the kidney always cause a discharge of purulent urine. The tumour may not involve the cavity of the kidney, or the ureter may be temporarily or permanently plugged. Thus the urine which is passed may all come from the other kidney and be quite normal. On the other hand, however, hæmaturia and pyuria associated with the physical signs of renal tumour are valuable adjuncts in forming a diagnosis.

To estimate the size of a renal swelling. As the patient lies on his back, place the fingers of one hand flat upon the ilio-costal space just outside the erector spinæ muscles, and those of the other hand flat on the front of the abdomen just over the hand which is behind. Then, during expiration, and whilst the patient's attention is diverted, a very fair idea will be obtained of the size and weight of the organ by depressing the fingers in front as much as possible, and tilting forwards those of the hand behind. In thin persons, and with the aid of an anæsthetic, [illegible] examination is very effective. [illegible] or diseased. Sir William Jenner points out that, when the lower dorsal and lumbar parts of the spine are curved well forwards, the kidney, even though only of natural size, may be sufficiently prominent to be seen through the abdominal parietes.

Diagnosis.—From enlargements of the liver.—Renal tumours often dip down or fade off so as to allow the fingers to be depressed between the edge of the costal cartilages and the upper border of the tumour. Hepatic tumours pass downwards from beneath the ribs, and so rarely do they have any intestine in front of them, the presence of bowel in front of a tumour may be regarded as a strong indication that it has not its origin in the liver. The presence of jaundice is an important indication.

A tumour developed in the concave part of the liver is very likely to cause error in diagnosis; especially hydatids in the left lobe of the organ, unless accompanied by jaundice.

On the clinical confusion between movable kidney, enlarged kidney, and tumours of the gall-bladder the reader is referred to a paper by the author in the *British Medical Journal* for 1895 (vol. i.)

From enlargements of the spleen.—The enlarged spleen has not bowel in front of it; it generally presents a sharp or well-defined edge, beneath which the fingers can be depressed; this edge is in some cases notched. There is resonance between the posterior edge of an enlarged spleen and the spinal column, and the tumour is traceable upwards beneath the ribs. A splenic tumour is movable; a renal tumour may be so, but often it is fixed in the loin. Splenic tumour will not cause varicocele, a renal tumour may do so.

Tumours of the suprarenal capsule cannot be distinguished clinically from those of the kidney; the absence of hæmaturia is an insufficient guide. The distinction, however, is not clinically of importance, since new growths of the suprarenal capsule, when of any consequence from their dimensions, involve the kidney, and sometimes completely efface it.

From ovarian tumours.—With an ovarian tumour the intestines lie behind; both loins are resonant; the tumour grows from below upwards, is generally more central, and either drags up the uterus, or can be felt as a swelling in the pelvis by vaginal or rectal examination. An ovarian tumour exceptionally has intestine in front of it: (i.) if of small size, the bowel may not be displaced backwards by it; (ii.) adhesions may be formed between a coil of intestine and the front surface of the tumour, so that the bowel retains an anterior position, as in a case of ovarian dermoid with twisted pedicle which I removed.

Enlargement of the lymphatic glands, in the near neighbourhood of the kidney, gives rise to a swelling very similar to a renal tumour. The diagnosis may be made sometimes by the independent enlargement of one or more lumbar glands not forming part of the tumour; by the abruptness of the outline of the swelling, and possibly even by a protrusion from the growth along the spermatic cord into the scrotum.

From carcinoma of the large bowel, from flatulent or fæcal accumulations in the cæcum, sigmoid flexure, or colon, renal tumours may be diagnosed by the absence of intestinal disturbance, of general abdominal pain and colic, of flatulent distension and intestinal obstruction.

The proximity of the colon to the kidney renders the diagnosis between nephritic colic and intestinal colic sometimes difficult. Sir William Jenner wrote: "Nephritic colic will cause loss of power in the colon, and so induce constipation, thus favouring the idea that the patient has intestinal colic. Again, collections of stools in the colon may be mistaken for an enlarged kidney; a large enema will solve all doubt on this point."

Fæcal abscess or perityphlitis will be distinguished by the marked febrile disturbance, the associated intestinal symptoms, the tenderness over the front surface of the part affected, and the lower position of the swelling, which will be in the iliac rather than in the renal region of the belly.

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REFERENCES

1. Barker, T. H. *On Cystic Entozoa in the Human Kidney.* 1856.—1*a*. Birkett. *Med Times and Gazette*, vol. i. p. 161, 1855.—2. Boeckel, Jules. *Studies on Hydatid Cysts of the Kidney.* Paris, 1887.—3. Bowditch. *Perinephric Abscess.* 1870.—4. Brodeur, Azarie. *Surgical Interference in Kidney Affections.* 1886.—5. Clarke, W. Bruce. *Diagnosis and Treatment of Diseases of the Kidney amenable to direct Surgical Interference.* 1886.—6. Courbis, E. *Cysts of the Liver and Kidney.* Paris, 1877.—7. Delafield, F. "Carcinoma," Pepper's *Medicine*, vol. iv.—8. Dickinson, W. H. *Urinary and Renal Diseases.* 1885.—9. Duplay and Reclus. *Traité de Chirurgie*, vol. vii. 1892.—10. Feron. *Perinephritis.* 1860.—11. Fischer, H. *Paranephric Abscess.* 1885.—11*a*. Fotheringham. *Brit. Med. Journ.* Dec 6, 1884.—12. Harrison, R. *Twentieth Century Practice of Medicine*, vol. i. 1895 Bibliography.—12*a*. Holmes *Path. Soc. Trans* vol. xxiv. p. 149.—13. Israel, James. *Operations on the Kidney.* Berlin, 1894 —14. Kraetschmar. *Des abscès périnéphriques.* Paris, 1872.—15. Lancereaux. *Encyclop. des Sciences medicales*, 1876. Art. "Reins."—15*a*. *Lancet*, Aug. 29, 1885.—15*b*. Le Dentu. *Affections chirurgicales des reins.*—15*c*. Legueu, Felix. *Calculs du rein et de l'uretère.*—15*d*. Lejars, Felix. *Gros rein polykystique.*—16. Liaudet, Jean. *L'Urétercctomie.* 1894.—17. Morris, Henry. *Diseases of the Kidney*, 1885; *Royal Med.-Chir. Trans.* vol. 59; *Brit. Med. Journ.* 1885; *Clinical Soc. Trans.*; *Lancet*, vol. i. 1888; *Brit. Med. Journ.* 1895, vol. i.—18. Newman, David. *Glasgow Medical Journal*, August 1883.—19. *Ibid.* *Lectures to Practitioners on the Diseases of the Kidney amenable to Surgical Treatment.* 1888.—20. Ralfe, C. H. *A Practical Treatise on Diseases of the Kidneys and Urinary Derangements.* 1885.—21. Rayer. *Traité des maladies des reins.* 1841.—22. Ritchie, James. *General Cystic Degeneration of the Adult Kidney.*—23. Rohrer, C. F. *Das primare Nierencarcinom.* 1895.—24. Roberts, W. *Urinary and Renal Diseases.* 1885.—25. Tuffier. *Études expérimentales sur la chirurgie du rein.*—26. Thornton, J. Knowsley. *Surgery of the Kidney.* Harveian Lectures, 1889.—27. Trousseau. *Clinical Medicine.*—28. Wynter and Wethered. *Clinical Pathology.* 1890.—29. Ziemssen, Von. *Encyclop.*

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NEPHROPTOSIS

MOVABLE OR FLOATING KIDNEY

Definition.—The kidney is said to be pathologically movable when by pressure, by alteration in posture, or by changes in the distension of the surrounding parts, it may be displaced from the position which it usually occupies.

Normal position.—There is a considerable variety in the exact site of the kidneys in their normal condition as observed in different individuals; but, in general, their position may be marked on the anterior wall of the abdomen in the following way:—The inferior pole of the right kidney is opposite a spot 3 cm. above a point 7 cm. from the linea alba on the horizontal line drawn through the umbilicus. The level of the superior pole is marked by a point 5 cm. from the linea alba on a horizontal line drawn on the abdominal wall 10 cm. above the horizontal umbilical line. The axis of the kidney corresponds to the line which joins these poles, and its hilum is on a plane internal to and below the edge of the eighth costal cartilage opposite the middle two-fourths of the axial line. The organ thus lies at the meeting-place of the hypochondriac, right lumbar, and epigastric regions as these are ordinarily defined. On the posterior wall of the abdomen the upper pole of the right kidney is 5 cm. external to the tip of the eleventh thoracic spine, and its lower pole is at a point 3 cm. above the iliac crest and 7 cm. external to the medio-dorsal line. The left kidney lies, usually, 1 cm. higher; and on each side the back of the kidney crosses the twelfth rib.

The kidneys are kept in their places to some small extent by the pressure of the surrounding viscera under the constraint of the muscles of the abdomen. The nature and amount of this constraining influence of the abdominal wall have been discussed by various authors. Schatz made the first formal attempt to demonstrate its existence, and its amount was calculated by Haughton; but, on account of the insufficiency of the experimental data employed, the results arrived at are not of practical value. Weisker (132), in an able paper, has demonstrated by his experiments, made in Ludwig's laboratory, that the intra-abdominal pressure in the sense of a retentive force is insignificant. The only demonstrable intra-abdominal pressure when the abdominal muscles are not actually contracting is the hydrostatic pressure of the viscera one upon the other. The viscera during life are soft and plastic; and, as they are closely packed together, by their mere weight they exercise a certain amount of pressure the one against the other; so that when hardened *in situ* they are mutually faceted and moulded upon each other. The right kidney presses against the back part of the abdominal wall posteriorly, and in front against the right lobe of the liver above, the colon below, and the duodenum and coils of the ileum along the mesial border. The left kidney is similarly compressed by the spleen and stomach above, by the pancreas medially, and by the jejunum and (to a small extent externally) the descending colon below.

The adipose capsule, which is the fatty and areolar envelope of the gland, acts as a semifluid pad around the organ. By dissection it can be made to appear as having a basis of rather firm connective tissue continuous inwards behind the kidney with the tunica adventitia of the aorta, and above with the subperitoneal tissue on the diaphragm. A layer of areolar tissue, without fat, continuous with this below, can be traced upwards over the ventral face of the kidney, beginning at the lower border of the gland and joining the deeper layer above. To this layer Englisch has applied the term "ligamentum suspensorium renis"; but the same structure was indicated, though much more indefinitely, by Bartholinus as the "fascia renum" two and a half centuries ago. The tissue of this capsule, which in the child is simply areolar, becomes filled with fat about the tenth year, more especially behind, below, and external to the gland; but this fat is much softer during life than it appears to be in the post-mortem room, and, as a retentive apparatus, the entire adipose capsule is of itself of but moderate importance. Tuffier (127) has carefully described this capsule.

The peritoneal reflexions, on the front of the kidney, act as the most important factors in the fixation of these organs. On the front of the right kidney the serous membrane is reflected from each side of the ascending colon; on the front of the left kidney, as Landau has pointed out, the serous reflexions from the upper and lower borders of the pancreas have a more definitely retaining influence. These attachments taken together, peritoneal and subperitoneal, are in general sufficiently strong to retain the kidneys in place in an opened abdomen when the cadaver is raised to the erect posture; and in only four out of twenty experiments did they permit of displacement from gravity. Upon the relations of these peritoneal folds and their retentive function the very important paper by Weisker (133) must be consulted.

Many forms of misplacement of the kidney, not attended with any considerable degree of mobility, have been described from time to time. The most important of these have been catalogued by Macdonald Brown and other authors. These malpositions are, for the most part, of anatomical rather than of pathological interest; they are seldom attended by any marked disturbances of function. In one instance, however, described by Hohl, a pelvic kidney was an obstacle to delivery. A similar case is recorded by Albers-Schonberg.

The kidney has normally a certain degree of mobility. Oncometric experiments show that the healthy organ varies in size with the varying conditions of blood-pressure, and of vascular dilatation and contraction (35). The surrounding organs are liable to corresponding variations; and, in consequence, the exact contour of the kidney, faceted by the pressure of neighbouring parts, is by no means constant. The condition ascertained in the bodies prepared by Professor Cunningham's ingenious method—in which the antero-external surface is transversely ridged between the hepatic and colic areas—represents a common but by no means an invariable result of this mutual visceral moulding.

Abnormal positions.—Almost all possible gradations in mobility have been observed, from the normal fluctuations in size due to the condition of the blood-vessels, and the normal alterations in position in the different phases of the respiratory cycle[1] and in different postures of body, to the extreme condition of "floating," in which the organ can be grasped by the fingers through the abdominal wall, and moved upwards and downwards by external pressure. Dr. Franks (37) recommends the following simple method of testing abnormal mobility. The patient being placed on the back, or else in the latero-prone position, the surgeon grasps the flank with his left hand, pressing his thumb in front below the costal arch and the fingers behind below the twelfth rib. If the kidney be abnormally movable it can be felt at the beginning of expiration below the grasp of the hand. If the right hand now press on the tumour when the left has relaxed its grasp the gland can be felt to slip upwards into its normal position. This method, however, is not always successful on account of the conditions of the surrounding viscera. Kuttner regards the deviations of every kidney which can be felt to move with respiration as pathological; but this view has been contested on sufficient grounds by Paul Wagner.

There are two structural conditions in which the kidney exhibits an abnormal degree of mobility. The rarer of these is that in which the kidney is partially or wholly enveloped in a mesonephric fold of peritoneum: to this form the name "Floating Kidney" is limited by Jenner and Newman. This anomaly is generally considered, but with insufficient reason, to be congenital: the possibility of the secondary production of a peritoneal fold is too well known to anatomists to exclude the possibility of the mesonephric fold being an acquired condition. Examples have been described by Girard, Roberts, Crum, Howitz, Priestley, Henderson, and Steven. In Steven's case there was undoubted evidence of displacement from tight-lacing. In an instance noticed in the dissecting-room, the peritoneum clothed the back of the right kidney and the upper end of the gland, reaching to the lower border of the hilum; but the lower border was not completely enveloped. The ascending colon was displaced nearly to the middle line, and the renal vessels were elongated and tortuous. Additional cases of the kind have been described by Franks (38) and others.

Cases of this kind cannot be clinically distinguished from those of the second form, and the methods of treatment are practically the same (Bruce Clark). If, however, the existence of a mesonephric fold be suspected, the method of operation should be by anterior abdominal section and intra-peritoneal fixation.

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[1] Landau (p. 244) denies the movement of the kidney with respiration, but Israel has both seen and felt these movements in lumbar sections (61).

In the majority of cases there is no mesonephric fold of peritoneum, and the gland moves within a lax areolar capsule. Hilbert distinguishes two grades of these cases: in the first only the inferior pole and not more than the lower half of the kidney can be felt; this he calls the "palpable kidney": in the second the whole kidney can be felt, and can be isolated with the fingers; this he calls the "movable kidney." Usually, however, the name movable kidney is indiscriminately used for examples of both grades (Jenner), and the condition of mobility has been named Nephroptosis.

This condition is met with at least seven times more commonly in females than in males. Kuttner asserts that one woman out of every five or six in the polyclinic of the Augusta Hospital, Berlin, had a pathologically movable kidney, but this must be taken in connection with his definition of mobility; indeed, this want of agreement as to the limit of normal and abnormal mobility vitiates all the statistics. Niehans finds it in about the same proportion in Berne. Mathieu found 85 cases out of 306 women examined in Paris (81). Dietl regards this condition as more common among the Poles than among other peoples; but the statistics given by Skórczewsky do not bear this out, as he only found movable kidneys in 3·1 per cent of 1030 females, and in 0·76 per cent of 392 males. Oser found that 10 per cent of the women whom he examined in Vienna suffered from this displacement.

Statistics of 300 cases show that the right kidney only was movable in 82 per cent; the left in 10 per cent; and both in 8 per cent. Of these 300 cases 87 per cent were females, and 13 per cent were males. Senator says that movable kidney is as common among the rich as among the poor, and he estimates that one case exists in every 139 of sick women. The majority of the women in whom this condition has been found were multiparæ; but in most of the cases which have been carefully noted the displacement appears to have begun at or shortly after the first pregnancy. It is most commonly met with between the ages of thirty and forty; but cases in children have been described by Hirschsprung, Keppler, Steiner, Wilks, Haward, Albarran, Drummond, Gilford, and others.

The character of the mobility is not always the same; the gland may slip up and down within the loose capsule, the motion being compared by Morris to "cinder-shifting" (86); or the kidney and its capsule may move on the hinder wall of the abdomen. In this case the gland may slip beneath the peritoneum, or the serous membrane may be attached to its surface anteriorly; but the marginal connections may be lax enough to allow of the gland moving forwards and inwards, dragging the membrane with it. Cases of this kind, such as those described by Jago and Gilford, simulate the true floating kidney. Indeed, it is so difficult to draw the line between them, that it is probable that some of the examples which have been referred to that group may really be of this nature.

These conditions are rarely noticed in the dissecting-room, owing to the position in which the body is dissected, and to the increased solidity of the adipose capsule after death. In the records of 6000 autopsies at the Berlin Charité, Landau found four cases only in which a movable kidney had been noted; out of 1600 at Guy's, Durham noted two only; out of 5500 at Oppolzer's Clinic, Rollet found twenty-two; and Sir Andrew Clark stated that he had met with only two examples in the course of 4000 post-mortem examinations.

The usual direction of the displacement is downwards, forwards and inwards; and, in slipping, the organ usually rotates so that the upper end and outer border move forwards, and the hilum is directed inwards and a little backwards; the extent of the motion being apparently limited by the length of the vessels. Adhesions or alterations in the surrounding viscera may lead to modifications in the direction of the displacement. The records of operation testify to the variety of positions which the gland may assume, such as those described by Urag and others. Mosler found the gland with the hilum directed upwards, and its convex border lying horizontally. All forms are usually associated with a medial displacement of the ascending colon, and the gland is usually below the level of the duodenum (Aberle). In many cases there is a remarkable absence of perinephric fat, but even this is by no means invariable (Durham).

Causes.—This displacement is not uncommonly associated with others, such as hernia or retroflexion of the uterus; sometimes it is part of the general relaxation of visceral connections named *Enteroptosis*, which has been described by Glenard, Ewald, and more recently by Grasset and Rauzier [*vide* art. "Enteroptosis," vol. iii. p. 587]. Landau noticed that in most of his cases the abdominal walls were flaccid; but the kidneys are not movable in all cases of pendulous abdomen. Any conditions which relax the abdominal walls certainly seem to dispose to this affection; and in this manner we can explain the mobility of the two kidneys noted by Siredey after hysterectomy. The range of motion varies from 3 or 4 cm. to 25 cm. In a case described by Dr. Bindley the kidney is described as moving under the peritoneum over a space which is called a circle with a diameter of 8 or 9 inches.

The predisposing causes are relaxation of the abdominal wall, diminution of the perinephric fat, and congenital elongation of the vessels. Indeed, it is probable that in most of the cases there has been some such congenital predisposition to the displacement; possibly, as Weisker has supposed, where a wide interval exists between the layers of the mesocolon, nephroptosis may be specially liable to occur. In the ancient description of dislocation of the kidney given in Pedemontanus' edition of Mesue's works, too frequent warm bathing is assigned as a predisposing cause (1581, p. 74 f.). The immediate cause of the dislocation may be a blow, a fall, a twist of the spine, or the carrying of a weight on the back when the body is bowed forwards, violent coughing, or straining in vomiting or parturition. Treves has seen a normal kidney worked out of its place by a vigorous masseuse who mistook it for a fæcal mass. There is no doubt of its frequent association with pregnancy, a change which disturbs the peritoneal relations of so many of the viscera;

and most cases are recognised for the first time when the abdominal parietes are relaxed after parturition. Gueneau de Mussy attempts to account for its being more commonly met with on the right than on the left by the supposition that the uterus rises more on that side. Landau believes the dragging influence of a colon distended with fæces to have some effect in the production of displacement; but this factor is undervalued by Champneys, the translator of his monograph (p. 279). Cruveilhier long ago pointed out the influence of tight lacing as a cause of displacement; and this cause has been reaffirmed by Bartels and Muller-Warneck; the latter blames also the laced bodices used in some countries. The objections of Landau (p. 275), who discredits the displacing influence of the stays, have been fully answered by Manassein, by Kuster of Marburg, and by Hertz; the last-named author shows that, in most cases, the tight-lace line on the liver is on the same level as the upper pole of the kidney. Thus pressure on the liver may be transferred to the right kidney and may dislocate it. The drag of heavy garments fastened round the waist also exercises a displacing influence; and Sophia Chamney has pointed out that this drag is even more injurious in the woman than it would be in the man; on account of the smaller lumbar curve and the greater shallowness of the bed of the kidney in that sex. The wearing of high-heeled shoes is also blamed by Von Korányi as predisposing to it by altering the lumbar curve.

In many cases, falls, fits of coughing, the jolting of carriage exercise, violent retching, and so forth, have led to the first recognition of the condition, if they have not been its producers (Henoch, Ferber, Le Ray, Defontaine).

Symptoms.—Out of 270 cases in which nephroptosis was determined by palpation, there were no symptoms of distress in 130; of the remainder, 72 suffered from various neuroses arising from the uneasiness felt in the kidney, from slight pressure effects, and from apprehension that this malposition might at any time give rise to more serious trouble; while in 68 the condition was accompanied by symptoms of a more serious nature (Curschmann). The sensation is one of weight and dragging with occasional colicky pains, and a sickening feeling when the kidney is pressed upon. This pain increases markedly during the incidence of the catamenia. Sometimes these sensations are intermittent, and have been compared by some patients to the sensation of quickening; indeed the symptoms have actually been mistaken for pregnancy (83). (See also Darányi.) In some cases the symptoms disappear during pregnancy, the enlarged uterus and the increase in the amount of retroperitoneal fat during that condition supporting the organ.

The catamenial aggravation of the characteristic sensations has been pointed out by Becquet, Lancereaux, Sawyer, and Fourrier; and has been regarded as indicating an etiological connection between the conditions: but although there is, as Virchow showed, a vaso-motor connection between the uterus and the kidney, yet it is difficult to see how any temporary increase of blood-pressure can cause permanent mobility. Guyon describes a case which first became noticeable in the menopause. In this connection a case published by Dr. Ferguson of Perth is particularly interesting.

The more troublesome effects of nephroptosis are twofold, disturbances of the digestive canal, and obstruction of the ureter or the renal vessel. Besides these there are certain pressure effects, such as "kidney-pain," in the knee, heel, or along the outer side of the thigh, and also along the genito-crural nerve in males, together with neuralgic pains in circumscribed areas of the body-wall; sometimes on the opposite side to that of the displaced kidney. In rare cases œdema of the right leg has been seen from pressure on the common iliac vein (Landau); while there is at least one case on record of thrombosis of the inferior vena cava (Girard) (43).

The disturbances affecting different parts of the digestive canal are sometimes very severe. Mathieu states that the percentage of cases of movable kidney in dyspeptics is very large; and it is well in cases of unaccountable disorders of digestion to search for the existence of nephroptosis. The symptoms are gastric pain, loss of appetite, frequent vomiting, and the other signs of gastric catarrh; the bowels are often obstinately constipated, the body becomes emaciated, and sometimes jaundice supervenes, lasting a few days, disappearing and recurring. In some cases the resulting exhaustion has almost proved fatal (Faulder White). In other instances intestinal obstruction has been attributed to renal pressure (Rollet, Dora). In others, again, obstinate fæcal accumulations were associated with nephroptosis (Kidd). The gastric symptoms, first described by Dietl in 1864, are liable to sudden and violent exacerbations, or "gastric crises," attended with abdominal tenderness, and sometimes with a slightly raised temperature. These symptoms last a day or two, disappearing if the patient continue recumbent; but are apt to return when the body reassumes the normal upright position. During the crises there is usually a transitory jaundice such as that described in Hale White's cases. In rare cases exacerbations of this nature have ended in peritonitis which has proved fatal (Berry). The appearance of the patient in several cases has been suggestive of malignant disease of the stomach, as described by Lochhead.

The amount of displacement is not necessarily commensurate with the severity of the symptoms. Edebohls has noticed that sometimes the cases with the most distressing symptoms are those in which the kidney has comparatively small range of movement.

Another series of disturbances may be met with in cases of nephroptosis. After some rapid or violent movement there is a sudden accession of intense and sickening pain; the abdomen becomes distended; the region of the kidney becomes excessively tender; giddiness, faintness, and sometimes delirium supervene; the pulse is small; the skin is covered with a cold sweat; the urine becomes scanty, dark in colour, and sometimes contains albumin and tube-casts. The symptoms increase for three or four days and then subside, recovery being generally accompanied by a copious flow of clear urine. These violent attacks have been attributed by Dietl and Ebstein to the wedging of the kidney into the subperitoneal tissue; and by Gilewski to acute hydronephrosis from the impaction of the kidney between the last rib and the vertebral column: and to them has been applied the name renal incarceration, from a supposed analogy with the strangulation of a hernia. Landau, however, from his own experiments, as well as from those of Robinson and of Perls and Weissgerber, has made the suggestion that they are due to torsion of the renal vein, as the pathological conditions are very like those which result from the experimental deligation of that vessel. Newman also in the course of several operations has verified the existence of this vascular torsion due to rotation of the kidney, giving rise to paroxysmal hæmaturia (95, 96). In these cases temporary albuminuria and tube-casts were due to mechanical hyperæmia; and Newman found in one case that the rotation of the kidney around its shorter axis had twisted the ureter and blood-vessels round each other.

Another series of distressing symptoms may arise from obstruction of the ureter occurring in a like manner from the rotation which accompanies the descent of the kidney. The same kind of kinking which has been described as affecting the veins must take place in the ureter; and this, by its frequent repetition, leads in process of time to dilatation of the pelvis of the kidney, and so to hydronephrosis. The process of dilatation has been carefully worked out by Landau, who has explained the mechanism of its occurrence. Cases illustrative of this effect have been described by Hare, Pernice, Ahlfeld, Cole, Clement Lucas, and Morris (87). In some of the 83 cases described by Terrier and Baudoin it is shown that the ureter has become permanently distorted by the occurrence of local inflammatory action, producing adhesions. For recent experiments on the mechanism of these intermitting hydronephroses, see Tuffier (128).

As a consequence of the interference with the vessels due to displacement, the movable kidney is liable to atrophy, this change being secondary to the displacement. In other pathological conditions in which the kidney increases in size and weight, displacement may take place, but this is only a secondary consequence of the enlargement. Thus tuberculous, carcinomatous, and sarcomatous kidneys may become movable and slip downwards. Calculi have also been found in displaced kidney, and consequent pyelitis has been described by Dickinson, Fritz, and Hickinbotham. While in general there is very little change in the nature and amount of the urine in nephroptosis (Rosenstein, Henoch) (54), yet sometimes there is periodic polyuria, as in the case described by Oppenheimer. Apolant accounts for this by supposing the nerves to be stimulated by the displacement.

As a collateral reflex concomitant of movable kidney tachycardia has been noted by Eccles. Certain conditions of the surrounding viscera have been occasionally found to accompany nephroptosis. The liver frequently shows deformation from the same causes which have caused the renal displacement, especially from tight lacing; and the kidney may be adherent to the anterior edge of its right lobe. The gall-bladder has been found dilated in a few instances (88).

But the most characteristic of these changes in neighbouring organs is the dilatation of the stomach which Bartels of Kiel has described, and attributes to the forward displacement of the gland pressing on the fixed descending portion of the duodenum, and so mechanically obstructing the normal passage of the chyme. This view is supported by Mathieu (82), Stiller, and Muller-Warneck. In Franks' case a peritoneal band from the upper portion of the kidney was attached to the duodenum in such a manner that, when the kidney was drawn down, the band dragged upon the duodenum and kinked it, thus practically occluding its lumen. Similar bands have been seen by Lenharz and Weisker, and I have been able to demonstrate the existence of folds of peritoneum of this nature in subjects in our dissecting-room. This condition, which would have been missed in Franks' case had the operation been performed retroperitoneally, is, I have reason to believe, not very uncommon, and furnishes a natural and adequate explanation of the gastric disturbances. Such bands may pass occasionally from the upper part of the duodenum, but they are more commonly attached to the middle or lower part of the descending portion, in the position nearly opposite that at which the bile-duct enters. The drag of the peritoneum on the duodenum is probably the commonest cause of the temporary jaundice which often accompanies the gastric crisis, and of the dilatation of the gall-bladder. The objections which Oser has brought against Bartels' hypothesis do not apply to that of Franks; on the contrary they rather favour it (100). Edebohls' opinion that the gastric crises are due to traction upon the nerves of the solar plexus (*loc. cit.*) is unsupported by any evidence, and is insufficient to account for the gastric enlargement and jaundice. Newman's suggestion that the jaundice is the result of concurrent biliary colic or catarrh of the bile-duct leaves the frequency of the coincidence unexplained; as does that of Lindner that the jaundice arises from a reflex spasmodic stricture of the bile-duct. It is improbable that the displaced kidney itself can ever press on the bile-duct or on the diverticulum Vateri as Litten supposed. Adhesion of a movable left kidney to the descending colon has likewise been met with as a result of circumscribed adhesive peritonitis.

Weisker, in the paper already quoted, has called attention to the close connection of the ligamentum hepato-duodenale to the bile-duct, which lies in its sharp border; and, as that fold is directly continuous with the peritoneal capsule of the kidney, it is difficult to imagine any very great displacement of the kidney taking place without an interference with the duct. Fischer-Benzon has described the coexistence of a dilated cæcum with nephroptosis.

Diagnosis.—Generally speaking, the diagnosis of movable kidney is not difficult; careful palpation by Franks' method usually suffices to detect the tumour. The peculiar sickening sensation when it is squeezed, and the position and form of the swelling, are characteristic. Sometimes there is a clearer percussion note than usual in the lumbar region (Guttman); but this is a very variable character. I have found the usual dull percussion note in a case in which the kidney was much displaced; and Landau has also noted the untrustworthiness of this sign. The conditions which most simulate it are those phantom contractions of the recti and internal oblique or transversalis muscles which appear as oval, smooth, definite tumours; but these resolve under chloroform, and although a movable kidney usually returns to its normal place under an anæsthetic, yet it is easy in such cases by bimanual palpation to ascertain the mobility of the gland.

There are no pathognomonic symptoms of movable kidney; but in cases where unaccountable gastric crises occur, or intermittent hydronephrosis can be diagnosed, a movable kidney may be suspected. As most of the conditions which are liable to be confounded with it show distinctive characters, in obscure cases, when the tumour itself is not distinctly palpable, the diagnosis is generally arrived at by a process of exclusion. Fæcal accumulations, hydrosalpinx, omental tumours, cancer of the colon, enlarged gall-bladder, the "tight-lace lobe" of the liver, ovarian tumours, and hydatid disease have all been taken for nephroptosis, but can usually with care be discriminated. On this subject Landau has made some acute observations. The diagnosis of enlarged gall-bladder from movable kidney is treated more fully in the chapter on "Diseases of the Gall-bladder" (p. 229).

Treatment.—The treatment of movable or floating kidney is twofold —palliative and operative. In cases in which there are no symptoms, or merely trivial neuroses, the constraint of a well-fitting tight jersey, put on before the patient rises from bed, careful attention to the bowels, and the avoidance of violent exercises, such as dancing and running, generally suffice to avert more serious discomfort. If these prove insufficient to fix the kidney, some more direct means of support may be used, such as a well-fitting abdominal belt extending from Poupart's ligament to the seventh rib, or Landau's abdominal stays with busks extending to the pubes. Massage has been recommended by Landau and by Eisenberg; and general treatment, especially ferruginous tonics, strychnine, and local douches or shower-baths, often proves of service.

Many forms of special retentive apparatus have been devised. Guéneau de Mussy suggested the use of an L-shaped pad beneath the abdominal binder, the horizontal leg being placed below, and the vertical external to the gland. Ellinger recommends a special form of bandage. Smith invented a truss with a straight spring—not oblique like that of a hernia truss; the posterior end is provided with four small pads which rest two on each side of the spinal column; and the anterior pad is a soft rubber air-cushion which can be inflated to the required degree of tension. A somewhat similar truss is recommended by Niehans (97), and a crescentic rubber air-pad has been devised by Stifler. A similar pad, invented by Bigg, is described in the *British Medical Journal* (11).

For local pains hot fomentations and sedatives may be used. Althaus has recommended the hypodermic injection of antipyrine; and the pain which sometimes supervenes in these mild cases from unwonted exercise generally subsides with rest, fomentations, poultices, and belladonna plasters.

When, however, the symptoms are severe, and retentive apparatus does not relieve them, or is not easily borne, surgical interference is called for. Two operations have been proposed—Nephrectomy and Nephrorrhaphy. The former has been advocated by Keppler, who regards a movable kidney as a continual menace to life; but it is a serious operation, and of the thirty cases recorded between 1870 and 1887 nine were fatal. The first recorded extirpation of a movable kidney was performed by Dr. Gilmore of Mobile, Al., in 1870. Of the fatal cases one is interesting, as the excised gland proved to be the only kidney possessed by the patient, who in consequence died of uræmia on the eleventh day (Polk). Meriwether more wisely sutured the solitary kidney in a case of displacement. Cases like that recorded by Hager are also calculated to make us hesitate to advise nephrectomy, except in those instances in which the displaced organ is hopelessly diseased. Adding in the more recent cases which have been recorded since the publication of Newman's list in 1888, the mortality of this operation up to date has been 23 per cent.

The operation of nephrorrhaphy—suture of the movable kidney to the abdominal wall—was introduced by Hahn in 1881; and was first practised in this country by Newman (94). This is a much safer operation; Keen has tabulated 134 cases in which it has been performed, out of which only four were fatal; Neumann has collected records of 274 cases, out of which only 1·82 per cent were fatal; and, still later, Albarran gives the statistics of 374 cases, showing a mortality of 1·87 per cent. These statistics justify the term "simple and safe," which Mr. Clement Lucas has applied to the operation. The French authors in general call the operation *nephropexia*, a name invented by Le Dentu, after the analogy of the name of *hysteropexia* applied to utero-fixation by Trelat.

The different methods of nephrorrhaphy have been experimentally investigated by Van der Lee and Triomi; but generally the operation is performed by the lumbar incision. The objects of the operation are to fix the kidney and its capsule to the abdominal wall, to attach the kidney to its capsule, and to reduce the size of the cavity in which the kidney moves. The incision needed is usually a little over 8 cm. long, and is carried from a point 1 cm. below the last rib close to the outer border of the erector spinæ, obliquely downwards and outwards towards the iliac crest; the fatty capsule is to be opened, and if loose a part of it should be cut away. Herczel, Tillmanns, and Lloyd have recommended the incising of the fibrous capsule so as to denude the cortical substance (9, 22). The operation requires to be varied to suit the case. M'Cosh points out that, according to circumstances, the fatty capsule may or may not be opened; it may suffice to pass the sutures through it, or, the fatty capsule being opened, the sutures may be passed through the fibrous capsule, or through the parenchyma of the gland; or the fibrous capsule may be partly stripped off. The incision described usually gives sufficient room for the subsequent proceedings; Ceccherelli, however, found it necessary to resect the eleventh and twelfth ribs, but his patient died from the consequences of his wounding the pleura. It is seldom necessary to drill the last rib and suture the gland to it, as was done by Lowson.[1] In one of Walther's cases where a reoperation was required, he found it desirable to suture the kidney to the costal periosteum. The sutures may be silk, kangaroo tendon, or silkworm gut; but they must be strong, as Newman has found that those which traverse the kidney substance are very rapidly destroyed. They are most conveniently inserted by the circular Hagedorn's needle. Newman uses a drainage-tube; but Morris recommends packing the wound with gauze or lint. Two to four stitches are usually enough, the sutures being inserted as widely apart as possible in the gland (Treves).

In cases where the diagnosis is doubtful, the intra-peritoneal operation is recommended by some (Herczel, *loc. cit.*), the incision being made in the linea semilunaris (Langenbuch). In a case thus operated on by Sir W. Stokes, adhesion took place without suture, as a result of the manipulation to which the kidney was subjected.

In all cases the patient must be kept recumbent for about six weeks after the healing of the wound, and should wear an abdominal belt for some time afterwards. The results of the operation as given by Albarran's statistics show that 64 per cent were completely successful, 14 per cent were partially successful, and 22 per cent were failures. In Neumann's list, 65·32 per cent are recorded as successful, 10·36 per cent were partially so, and 22·07 failed.

Some modified operative procedures have been recommended by other authors. Riedel has introduced a method of fixation to the diaphragm which, although advocated by Reineboth, does not seem to possess any advantage. Mikulicz, by painting the peritoneal surface with iodoform collodion, has succeeded in producing a circumscribed adhesive inflammation so as to fix the viscera together. In case adhesions of the kidney to any of the viscera are found in the course of the operation, Sulzer recommends that care be taken not to stretch them unduly; permanent traction is apt to be followed by persistent pain. When nephroptosis is a part of a general condition of enteroptosis it must be treated accordingly (Treves (125), De Renzi) [see also article "Enteroptosis," vol. iii. p. 587]. The treatment of hydronephrosis, when complicated by mobility, differs in little from that occurring when the gland is in its normal site [see article "Hydronephrosis," p. 430].

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[1] Albarran recommends that the length of the twelfth rib should be ascertained before operating, as he believes that if it be unusually short there is danger of wounding the pleura. This, however, is only an occasional danger, as in seventeen cases in which this rib was under 6 cm. in length, the pleura was as far as usual from the track of the needle. Holl and Lange have, however, found that in some cases the pleura does descend as far in such instances as in those having the normal length of rib, and Dumreicher has actually opened the pleura in operation on an enlarged kidney.

REFERENCES

1. ABERLE. *Salzburger medic.-chir. Zeitung*, 1826, iv. 253.—2. AHLFELD. *Archiv fur Gynakologie*, 1879, xv. p. 114.—3. ALBARRAN. *Annales des maladies genito-urinaires*, Aug. 1895.—4. ALBERS-SCHONBERG. *Centralblatt fur Gynakologie*, xviii. 1894, No. 48.—4*a*. ALTHAUS. *British Medical Journal*, 1893, vol. i.—5. APOLANT. *Deutsche medicinische Wochenschrift*, xii. 1886, No. 41.—6. BARTELS. *Journal de médecine et de chirurgie pratiques*, 1884, lv. p. 394.—7. BARTHOLINUS. *Anatomie*, 1673, p. 177.—8. BECQUET. *Arch. gén. de méd.* Paris, 1865, v. p. 5.—9. *Beitrage zur klinischen Chirurgie*, 1892, ix. p. 648.—10. BERRY. *New Orleans Medical and Surgical Journal*, July 1889, p. 45.—11. BIGG. *British Medical Journal*, 1896, i. p. 1368.—12. BINDLEY. *Transactions of the Pathological Society of London*, xxvii. p. 173.—13. BROWN, MACDONALD *Journal of Anatomy*, xxviii. p. 194.—14. CECCHERELLI. *Rivista Clinica*, April 1884—15. CHAMNEY, SOPHIA. *Inaugural Dissertation.* Berne, 1893.—16. CLARK, BRUCE *British Medical Journal*, 1895, i p. 577.—17. COLE. *British Medical Journal*, 1874, i. p. 453.—18. CUNNINGHAM. *Journal of Anatomy*, July 1895, p 501.—19. CURSCHMANN. *Schmidt's Jahrbucher*, ccxxviii. 1890, p. 115.—20. DARÁNYI. *Gyógyászat*, Budapest, 1880, xx. p 382.—21. DEFONTAINE. *These sur la Pathologie des reins mobiles.* Paris, 1871.—22. *Deutsche Zeitschrift fur Chirurgie*, 1892, xxxiv. p. 627.—23 DICKINSON. *Renal and Urinary Affections*, vol. iii.—24 DIETL. *Wien. med. Woch* xiv. 1864, p. 563.—25. DORA. *Philadelphia Medical and Surgical Reporter*, 1879, xl. p. 502.—26 DRUMMOND. *Lancet*, 1890, i. p 68.—27. DURHAM. *Guy's Hospital Reports*, 1860, p. 404.—28. ECCLES. *British Medical Journal*, 1890, i. p. 1250.—29. EDEBOHLS *American Journal of Medical Science*, cv. 1823, No. 4.—30. ELLINGER *Wiener medicinische Wochenschrift*, 1881, xxxi. No. 17, p. 1315.—31. ENGLISCH. *Deutsche Zeitschrift fur Chirurgie*, Leipzig, 1879, xi. p. 28.—32. EWALD. *Berliner klinische Wochenschrift*, xxvii. 1890, No. 12.—33. FERBER. *Virchow's Archiv*, lii 1871, p. 95.—34. FERGUSON. *Glasgow Medical Journal*, 1889, xxxi. p. 348.—34*a* FISCHER-BENZON. *Thesis zur Anatomie d. bewegl. Niere.* Kiel, 1887.—35. FOSTER *Physiology*, 6th edit iii. p. 689 *sqq.*—36. FOURRIER. *Bulletin générale de Thérapeutique*, lxxxviii. June 1875, p. 481.—37. FRANKS, KENDAL. *British Medical Journal*, 1895, ii. p 895.—38. *Idem.* *Transactions of the Royal Academy of Medicine of Ireland*, 1893, p. 392.—39. FRITZ. *Archives générales de médecine*, 1859, ii. p. 158.—40. GILEWSKI. *Wiener medicinische Wochenschrift*, 1865, xv. 596.—41. GILFORD. *Lancet*, 1893, ii. p. 1559.—42. GIRARD. *Gaz. méd. de Paris*, 1837, p. 89.—43. *Ibid.* *Journal hebdomadaire de progrès des sciences médicales*, 1836, iv. p. 445.—44. GLÉNARD. *Lyon médical*, 1885.—45. GRASSET and RAUZIER. *Maladies du système nerveux*, Paris, ii. 104.—46. GUTTMAN. *Physical Diagnosis*, Sydenham Soc 1879, p. 364.—47 GUYON. *Journal de médecine et de chirurgie pratiques*, 1888, p. 441.—48. HAGER. *Berliner klinische Wochenschrift*, Aug. 1889, xxvi.—49. HAHN. *Centralblatt für Chirurgie*, 1881, viii. July 23, p. 449.—50. HARE. *Medical Times and Gazette*, xvi. 1858, pp. 7, 112.—51. HAUGHTON. *Animal Mechanics*, 1873, p. 218.—52. HAWARD. *Med.-Chi. Tr.* 1888, lxxi. p 81.—53. HENDERSON. *Medical Times and Gazette*, 1859, ii. 501.—54. HENOCH. *Klinik der Unterleibskrankheiten*, iii. p. 367—55. HERTZ. *Abnormitaten der Bauch-organe.* Berlin, 1894.—56. HICKINBOTHAM Quoted by Greig-Smith, *Abdominal Surgery*, 1891, p 523.—57. HILBERT. *Archiv für klinische Medicine*, l. 1892, p. 483.—58. HIRSCHSPRUNG. *Hospital-Tidende*, Copenhagen, 1879, vi. 949.—59. HOHL. *Meckel's Archiv*, 1828, p. 355.—60. HOWITZ. *Hospital-Tidende*, xvi. 1873, 14, p. 53.—61. ISRAEL. *Berliner klinische Wochenschrift*, xxvi. 1889, Nos. 7, 8.—62. JAGO. *Medical Times and Gazette*, 1872, ii p. 328.—63. JENNER. *British Medical Journal*, 1869, p. 43.—64. KÉRR. *Transactions of the American Surgical Association*, 1890, p. 197.—65. KEPPLER. *Archiv fur klinische Chirurgie*, xxiii. 4, 1879, p. 520.—66. KIDD. *Lancet*, 1894, ii. p. 131 ; 1895, ii. p. 1564.—67. KORÁNYI, VON. *Berliner klinische Wochenschrift*, 1890, No. 31.—68. KUSTER. *Lancet*, 1895, i. 1077.—69. KUTTNER. *Berliner klinische Wochenschrift*, xxvii. 1890, Nos. 15-18.—70. LANDAU. New Sydenham Soc. 1884, cx. p. 278.—71. LANDAU and EISENBERG. *Wiener med. Presse*, 1891, xxxii. No. 36.—72. LANGENBUCH. *Deutsche medicinische Wochenschrift*, 1889, xv. No. 16, p. 325—73. LEE, VAN DER. *Leyden Dissertation*, 1893.—74. LINDNER. *Deutsche medicinische Wochenschrift*, 1884, x. p. 230.—75. LITTEN. *Berlin Charité Annalen*, 1880, p. 10.—76. LOCHHEAD. *Glasgow Medical Journal*, 1896, xlv. p. 420.—77. LOWSON. *British Medical Journal*, 1893, i.

p. 11.—78. Lucas, Clement. *British Medical Journal*, 1891, ii. p. 1343.—79. M'Cosh. *New York Medical Journal*, March 15, 1890, p. 281.—80. Manassein. *Vratch*, 1887, viii. p. 206.—81. Mathieu. *Ann. des malad. génito-ur.* xii. 1894, p. 70 — 82. *Idem. Progrès médical*, Oct 29, 1892.—83. *Medical Times and Gazette*, 1869, ii. 32.—84. Meriwether. *Annals of Surgery*, Sept. 1891.—85 Mikulicz. *Zeitschrift fur Gynakologie*, 1890, xix. p. 358.—86. Morris. *British Medical Journal*, 1892, i. p. 1009.—87. *Idem. Medico-Chirurgical Transactions*, lix. p. 227.—88. *Idem.* 1895, i. p. 238.—89. Mosler. *Berliner klinische Wochenschrift*, 1866, iii No. 141, p. 393.—90. Müller-Warneck. *Berliner klinische Wochenschrift*, xiv. 1877, No. 30, p. 429.—91. Mussy, Guéneau de. *Clin. méd.* 1875, ii. p. 187.—92. Neumann. *Inaugural Dissertation.* Berlin, 1892.—93. Newman. *Glasgow Medical Journal*, 1883, xx. p. 85.—94. *Idem.* August 1883, p. 121.—95. *Idem. British Medical Journal*, 1896, i. 149 —96. *Idem. Lancet*, 1896, ii. p. 1758.—97. Niehans. *Centralblatt f. Chir.* xv. 1888, No. 12.—98. Oppenheimer. *Deutsche medicinische Wochenschrift*, xvi. 46, 1890.—99. Orum. *Gynak. og Obstet. Meddelelser*, Copenhagen, 1879, ii. pp. 307-388.—100. Oser. *Wiener med. Klinik.* 1881, i. p. 1.—101. Pernice. *Deutsche medicinische Wochenschrift*, 1879, No. 9.—102. Polk. *New York Medical Journal*, 1882, vol. ii.—103. Priestley. *Medical Times and Gazette*, 1857, p. 263.—104. Ray, Le. *Thèse des reins mobiles.* Paris, 1876.—105. Reineboth. *Inaugural Dissertation* Jena, 1892.—106. Renzi, de. *Riforma Medica*, Dec. 22, 1894.—107. Riedel. *Berliner klinische Wochenschrift*, 1892, xxix. No. 28.—108. Roberts. *Urinary and Renal Diseases*, 1885, p. 672.—109. Rollet. *Pathologie und Therapie der beweglichen Niere.* Erlangen, 1866.—110 Rosenstein. *Nierenkrankheiten*, p. 374.—111. Sawyer. *Birmingham Medical Review*, 1872, i. p. 116.—112. Schatz. *Archiv fur Gynakologie*, iii. 1, 1871, p 174.—113. Senator. *Deutsche Medicinal-Zeitung*, 1883, p. 479.—114. Siredey. *Bulletin et mémoires de la société médicale des hôpitaux de Paris.* October 26, 1893.—115 Skórczewsky. *Przeglad Lekarski*, Krakow, 1882, xxi 3. 20.—116. Smith. *New York Medical Journal*, 1883, xxxvii. p. 183.—117. Steiner. *Compendium der Kinderkrankheiten*, 1872, p. 311.—118 Stevens. *Glasgow Medical Journal*, xx. 1883, p. 307.—119. Stifler *Munchener medicinische Wochenschrift*, 1892, xxxix. No. 28.—120. Stiller. *Wiener medicinische Wochenschrift*, 1879, xxix. No. 4.—121. Stokes, Sir W. *British Medical Journal*, 1895, i. p. 853.—122 Sulzer. *Deutsche Zeitschrift fur Chirurgie*, xxxi 1891, p. 506.—123. Terrier and Baudoin. *Revue de chirurgie*, 1891, ii. 719.—124. Treves. *Lancet*, 1896, i. 17.—125 *Idem. British Medical Journal*, 1896 i p. 1.—126. Triomi *Mercredi médical*, May 23, 1894.—127. Tuffier. *Revue de chirurgie*, x. May, 1890, p. 390.—128. *Idem Annales des Maladies génito-urinaires*, 1894, xii. p. 14.—129. Urag. *Wiener medicinische Wochenschrift*, 1857, No. 3.—130 Virchow. *Monatschrift fur Geburtskunde*, 1857, x. p. 242.—131. Walther. *Revue de chirurgie*, 1893, x p. 273.—132. Weisker *Schmidt's Jahrbucher*, ccxix. 1888, p. 277.—133. *Idem* ccxx. 1888, p 249.—134. White, Faulder. *British Medical Journal*, 1895, i. p. 1376.—135. White, Hale. *British Medical Journal*, 1892, i. p. 223.—136. Wilks. *Lancet*, 1862 ii. 139.

137. Abbott. *Boston Med. and Surg Journ* 1864, p. 439.—138. Le Dentu. *Affections chirurgicales des reins.* Paris, 1889 —139. Desme. *These des reins flottants.* Montpellier, 1885.—140. Duvel. "Du traitement des reins mobiles par la néphrorrhaphie," *Bull. de l'Acad. Roy. Méd. de Belg* v. 1888, p. 440.—141. Guyon. "Les déplacements rénaux," *Gazette des Hôpitaux*, 1892, lxv. 103.—142. Hare. "Report of Pathological Society on Movable Kidney," *Tr. Path. Soc.* 1875, xxvii. p. 467.—143. Hfrr. *Die wandernde Niere.* Frankfort a M. 1871.—144. Keen. "Nephrectomy," *Philad. Med. News*, lvii. 18, 1890.—145. *Idem.* "Nephrorrhaphy," *Boston Med. and Surg. Journ.* 1890, cxxii. 23.—146. Martineau. *Des reins flottants*, Thèse, 1868.—147. Pieper. *Ueber Cystenbildungen beweglicher Nieren.* Berlin, 1867.—148. Schultze. *Zur Casuistik der bewegl. Niere.* Berlin, 1867.—149. Serres. *De rene quem dicimus errantem.* Greifswald, 1866.—150. Thun. *Ueber bewegliche Niere.* Berlin, 1869.—151. Tzschaschel. *Ueber bewegl. Niere.* Berlin, 1872.

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DISEASES OF THE KIDNEY CHARACTERISED BY ALBUMINURIA

THE present article deals with the diseases of the kidney which are ordinarily indicated by the presence of albumin in the urine. The name albuminuria is too comprehensive, for it is not proposed here to include functional or cyclic albuminuria, or that of adolescents, or any of the conditions of which hæmorrhage is the essential characteristic though albumin may at times be present without the other constituents of blood. Nor does the term Bright's disease exactly fit. This description covers much of the subject, but not the whole. The denomination has by common usage, for which the public are mainly responsible, become restricted to the more chronic and persistent varieties. To say of a person with a temporary nephritis that he has Bright's disease would give a false impression, create unnecessary alarm, and convey a sentence of death to one not doomed to die. The topic in hand cannot be more tersely defined than as diseases of the kidney characterised by albuminuria. These may be broadly divided into three groups, though the demarcations are not sharply defined, for the conditions run more or less into each other and present a certain amount of intermixture. The broad divisions are as follow:—

I. NEPHRITIS, TUBAL, DIFFUSE, AND GLOMERULAR.—We have here the immediate results of inflammation, which may affect the tubes only or involve also the interstitial tissue or the Malpighian bodies. This state of the organ is generally attended with congestion and increase of bulk, the latter chiefly in the cortical tissue. The congestion is most marked in the early stages, the swelling in the later. The surface long remains smooth, at any rate until contractile changes are superadded which may eventually give rise to superficial unevenness and remove the condition into the second class, that of the granular kidney. The climax of the first class is reached in the large white kidney of nephritis.

II. THE GRANULAR OR CIRRHOTIC KIDNEY.—This may arise as the sequel of acute interstitial inflammation; or, what is more common, may present itself as the result of gradual, insidious changes, no doubt inflammatory in their essence, but so obscure in their beginning and latent in their progress that no inflammatory outbreak can be discerned in their origin or course. The leading characteristic of this organic state is contraction, of which superficial granulation or minute nodulation is the sign. The contractile process may lessen or supersede an antecedent increase of bulk, or, as more often happens, may occur without it, the organ beginning to shrink from the first.

III. THE KIDNEY OF LARDACEOUS DISEASE, OTHERWISE DESCRIBED

AS WAXY OR AMYLOID.—This commonly occurs together with changes of the same nature elsewhere. The essential fault is a deposition within the organ of a peculiar substance which is different from all the normal components of the body, and is best detected by its reaction with iodine. The alterations in the kidney present a great variety, and have already been described. [See vol. iii. p. 259.]

The lardaceous process is apt to set up in the kidney various inflammatory and fibrotic changes, which consequential complications impart to the organ many of the characters which belong to nephritis and granulation.

It will be observed that I have not mentioned the *fatty kidney* as a substantive or independent condition. The renal epithelium may become charged with oil in a variety of circumstances; it is often so, even to a considerable extent, without any interference with the renal functions, in connection with states which concern the whole body. With tuberculous disease, such as phthisis, it is often so. With many conditions which affect the kidney locally the epithelium often displays this state to an extreme degree. It is often so with nephritis, particularly when this is due to cold; after scarlatina there is little tendency to fattiness. With the granular kidney the fatty change may be presented, and with the lardaceous the epithelium is sometimes loaded with oil to the extreme of possibility, while at other times it is free. There is a close association between fatty and lardaceous change, as is often seen in the liver. Alcoholic drinks, particularly beer, tend to make the kidneys fatty, whether in connection with other renal alterations or without them. The peculiar action of phosphorus in producing fatty degeneration of the kidney, as well as of other organs, need not here be dwelt upon.

I. NEPHRITIS.—**Morbid anatomy.**—Before proceeding to clinical considerations, I will say as much concerning the morbid anatomy of the disease as is necessary for the understanding of its course and symptoms. Many pathological details, which need not be recapitulated here, will be found in another part of this work. Unlike many other diseases, the definition of nephritis lies in its morbid anatomy, which may therefore be properly considered before its clinical manifestations.

The more closely we regard the results of this disease the less simple we find them to be. Inflammation, which notably involves the tubes and is revealed to us only by their means, is apt to be shared by the interstitial tissue, and to display after death a complex condition. It is not possible, therefore, to deal with the varieties of nephritis with academic distinctness, nor can we assume exact limitations which nature does not present.

Nephritis may be acute or chronic, with many degrees of intensity or protraction.

To take, first, the acute form, as commonly presented two or three weeks after its outset, the result of cold, scarlatina, or diphtheria, the kidney may be thus described. It is increased in weight and bulk, but not to the extent attained by the large white kidney of chronic disease In an extreme case, particularly of the congestive variety, the weight may be doubled or even more; but usually the increase is in much smaller proportion. The surface remains smooth, and the capsule thin and unadherent. The organ is everywhere, even including the pelvic mucous membrane, hyperæmic. The capsular surface is injected especially as to the minute intertubular network; stellate veins belong to a later period The whole organ on section exudes blood freely, and the cortex is uniformly besprinkled with conspicuous red specks, which are injected Malpighian bodies; the hyperæmia of the cortical substance is to a certain extent masked by its infiltration with a pale or buff material which chiefly consists of a superabundance of epithelium.

The most striking change, as viewed with the microscope, is the obstruction and distension of the tubes, which are stuffed with epithelium, granular matter, and often blood and fibrin; to the more or less obliteration of their channels. Sometimes the fibrin is so abundant as to occupy most of the tubes to the exclusion of their epithelial lining, lying in immediate contact with the basement membrane—the situation suggesting that the adventitious material is an exudation from the tube walls rather than an escape from the Malpighian bodies. The general sealing up of the renal exits which results is necessarily attended with corresponding diminution of urine.

In many of the more intense, the more protracted cases, and often the scarlatinal cases, the intertubular substance shares in the inflammatory process, and displays hypernucleation and new fibroid growth. The new growth is more or less uniformly distributed between the tubes, in which respect the fibrosis of acute nephritis differs from that of the chronic granular kidney, where it presents itself in processes.

There are many grades in the condition of nephritis, and much variation in the amount of change which appeals to the naked eye Sometimes this is so little conspicuous that though the renal disturbance may have been sufficiently evident during life, yet after death it might be overlooked by a careless observer. In other cases the disorder leads to organic alterations so obvious that it is a marvel that they so long escaped record. I have preferred to place first the conditions most frequently met with; I now come to one which is less common but more striking Sometimes, particularly when the attack is the result of a definite exposure to cold, and the subject middle-aged and intemperate, an acute form of nephritis manifests itself which is characterised by extravagant congestion, even to chocolate or purple, and great and rapid swelling of the gland; so that, as I have seen at least in one instance, the kidneys have burst their capsules. Short of this exceptional result, the whole organ, but chiefly the cortical tissue, is enormously swollen, the cortex changed to a deep coffee colour, and the cones to purple, while the tubes are distended chiefly with epithelium and blood. If the blood be removed by washing, the cortical tissue will show, what before was obscured, a finely-divided superaddition of a buff colour. An admirable representation of this form of kidney is to be seen in Bright's classical work. I have elsewhere recorded in detail the case to which I have already referred, in which the capsules were torn open by the swelling of the gland. It will be seen by the illustrations which I have elsewhere published that the interstitial tissue, both in the cortex and cones, was profusely charged with a new corpuscular formation. It was not impossible that in this case the intense nephritis may have been associated with hæmoglobinuria.

It must not be passed without notice that in certain cases of diffuse nephritis, particularly of scarlatinal origin, the Malpighian bodies are especially involved to the extreme diminution of the urine, and the name glomerular nephritis is applied to the condition. This is characterised by uræmia rather than dropsy. The change may occur in the course of scarlatinal nephritis, while as yet the inflammatory process is but incipient in the tubes and general interstitial tissue. There is a copious nuclear formation within the Malpighian capsule by which the contained vessel may be compressed, the capsule is thickened by a similar growth, and there is hyaline degeneration of the Malpighian coil. The change conveys the suggestion that Malpighian structure is early and intensely affected by some irritating property in the scarlatinal blood or in the urine which here takes its origin from it.

Passing from the acute to the chronic we reach the large white kidney of nephritis. "The large white kidney," and that in a most typical shape, may also be a result of lardaceous disease; the term, therefore, is not distinctive unless the qualification "of nephritis" be added. The large white kidney of nephritis is a sufficiently striking manifestation of renal disease. The organ is increased even to three times its normal weight. The surface as yet remains smooth. It is abnormally pale, the pallor of the surface relieved by stellate veins or indefinite patches of congestion. The cortex on section is seen to be similarly pale and greatly increased in bulk. The cones are likewise increased, but to a less extent; they retain much of their normal red colour, so that the contrast between them and the pale or buff cortex is far beyond what the healthy kidney presents. The condition is the issue of a general or diffuse nephritis which affects both the tubes and the intertubular substance. The tubes are variously distended and obstructed, and the material between them hypertrophied, hypernucleated, and beset with the fibrillæ of new fibroid tissue.

The next phase, which is one of slow and infrequent attainment, is the conversion of the large smooth kidney into the contracted and granular. The new fibroid tissue gradually contracts, as its manner is, draws in the surface at numerous points of attachment, and narrows and strangulates the tubes which it involves. The resulting condition, one of contracting fibrosis, is essentially the same as that of the granular kidney of gradual accession, though there are differences of appearance which point to the differences of origin. With the ordinary granular kidney the change begins upon the surface with a fine and regular granulation, and slowly reaches the inner parts, which long retain much of their natural colour and texture. As the sequel of acute disease a superficial unevenness in the shape of scattered indents or depressions is superimposed upon the preceding general change. The unevenness may in course of years attain to something of general granulation, but this is seldom so regular as in the contrasted condition. Even then there remains much of the original white or buff colour, and of cortical excess, particularly in the deeper parts; so that many of the internal characters of the large white kidney are still to be found in association with the granulated surface of contracting fibrosis.

For purposes of classification, dealing with the kidneys as displayed post-mortem, nephritis is better defined by naked-eye observation than by microscopic. The microscope will show various forms of disturbance in the tubes and their contents; it may or may not display the results of interstitial inflammation in hypernucleation or overgrowth, since they may be present or absent according to the cause and intensity of the attack. The question whether the inflammation is confined to the tubes, or affects also the intertubular substance, does not enter into the definition. The kidney of nephritis must be defined partly by negatives: it gives no lardaceous reaction; it is not contracted, or at least not so much contracted as to entitle it to be classed as contracted and granular, which state nephritis may ultimately lead to. The surface remains smooth, or nearly so; the cortex is increased, often greatly. The disease attains its extremes, as the swollen chocolate kidney of acute inflammation, and the large white mottled kidney of chronic disease; beside and between which there are a variety of intermediate states characterised by increased cortex and smoothness of surface.

Sex and Age.—First with regard to *sex*—all forms of albuminuria are more common in males than females. With nephritis this difference exists at the earliest periods and increases as age advances. In early life, when nephritis is largely due to scarlatina, the difference is apparent. Dr. Tripe, writing of scarlatinal dropsy, gave the proportion of males to females as 60 to 39. Of 105 cases of nephritis from all causes in children under 12 years of age, at the Hospital for Sick Children, 58 concerned boys, 47 girls. Later the preponderance is on the same side. Taking adults, that is, persons over the age of 16, and appealing to 54 cases under my own observation, I find that there were 33 male subjects, 21 female.

The greater prevalence of albuminuric disease, connected as it so often is with inflammatory action whether acute or chronic, in the male is only what would be expected. An organ is perhaps liable to disease of this nature in some sort of proportion to its activity of function; it is certain that it is so liable in proportion to its subjection to morbid stimulation. The man habitually throws more work upon the kidney in eating and drinking than does the woman. He is more exposed to weather than she is, he has a greater propensity to gout, and he is more conversant with lead. There is one cause of renal disease which affects the female only, to wit, pregnancy; but this is not enough to counterbalance the other causes of renal disease.

Next as to *age*. The disease preponderates in early life, though perhaps no age can claim exemption. It is nearly unknown in the first year, rare in the second, afterwards common up to the beginning of old age. The frequency with which it happens in children as the consequence of scarlatina or cold must have struck every one who is familiar with the diseases of childhood. As to its occurrence in later life it may be stated to be rare after 40, not unknown after 50. The cases admitted into a general hospital like St. George's do not fairly present the proportion of children affected, since so many of these find their way into hospitals special to them; the following figures, therefore, understate the occurrence of the disease in childhood. With this qualification they may be of value. Of 44 fatal cases of nephritis at St. George's under my own observation, all of them certified by post-mortem examination, the ages at death were as follows:—under 10 years, 12; from 10 to 19, 7; from 20 to 29, 10; from 30 to 39, 9; from 40 to 49, 4; from 50 to 59, 2. The oldest patient was 56 years of age.

Causes.—As *predisposing* causes several present themselves—climate, heredity, drink, and mental or nervous exhaustion. Climate has a paramount, overruling influence. Inflammatory conditions of the kidney are more frequent in temperate climates than with the extremes of either heat or cold, so that a medium temperature may be held to conduce to inflammation of the kidney, as a temperature of the tropics conduces to that of the liver. At the same time a hot climate is by no means a preventive, for I have known acute nephritis to have been brought on in hot weather in India by keeping on wet clothes or long sitting in a cold bath. With regard to heredity, I may refer to a remarkable instance in which chronic albuminuria declared itself in four generations and fifteen individuals of an ancient family. From such post-mortem evidence as was obtainable, and from the fact that one of this stricken race[1] got completely rid of his albuminuria after having had it for many years, it was inferred that the disease was a very chronic form of nephritis. It might be debated whether in this case the hereditary tendency should not rather be called the exciting cause than the predisposing, for at least one of the subjects presented albuminuria at birth. Leaving the verbal question as of no importance, it is certain that heredity is a potent factor in the production of nephritis.

The especial liability of drunkards to be attacked with acute nephritis on exposure to cold, seems to warrant the placing of alcoholic intemperance among the predisposing causes of this disease. Among the circumstances which, I think, predispose to nephritis are mental depression and nervous exhaustion. I have known this disease to come on under such circumstances from causes which would seem otherwise inadequate.

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[1] *Occasional Papers on Medical Subjects*, W. H. Dickinson, p. 150.

that I cannot doubt that the renal susceptibility is increased by nervous or constitutional depression.

I have satisfied myself that the tubercular diathesis has no special association with nephritis. Before lardaceous disease was differentiated, it was common in the post-mortem room to hear a large white kidney called scrofulous. There might be some excuse for thus characterising the kidney of this type when it was lardaceous, and the result of scrofulous disease; but the kidney of nephritis proper is not more apt to present itself in tuberculous persons than in others.

Coming to the *exciting or immediate causes of nephritis*, it would be possible, were we to include the more chronic varieties, to give a list which should contain most of the causes of the granular kidney, as well as of what is generally recognised as nephritis, for the granular kidney is virtually a late result of nephritis in a chronic form. But I will restrict myself to nephritis in its more acute form according to the general use of the term. This limitation will exclude gout, which appears to have little to do with the acute forms of renal disease, however much it may be concerned with the chronic.

The exciting causes of nephritis may be briefly classed as unnatural or excessive stimulation of the glandular function, irritation of the organ possibly not directed especially upon the secreting function, undue determination of blood to the organ, or retention of blood in it.

In detail the causes may be thus specified:—

1. Circumstances which throw upon the kidney the work of other glands. Cold to the surface of the body, by checking perspiration, directing upon the kidney what should escape by the skin, and driving the blood from the surface inwards. Obstructions to the escape of bile, whence this irritant has to be vicariously eliminated by the kidney. Diabetes, which pours sugar, which is a renal irritant, upon the channels of urinary elimination. Destruction of one kidney, whereby double work is thrown upon the other.

2. Diseases which develop a renal irritant—scarlatina, measles, diphtheria, erysipelas, septic disease, typhus, pneumonia, cholera (?), acute rheumatism (?).

3. Matters taken from without which act as renal irritants: turpentine, cantharides, alcohol, lead, arsenic, etc.

4. Conditions which act directly upon the renal circulation. Pregnancy, by obstructing the venous exit; that this state interferes with the kidney in some other way is probable, the mechanical process admits of no doubt. Valvular disease of the heart, by causing venous congestion—less renally mischievous than pregnancy. Malarial disease, by driving the blood from the surface to the deep organs.

Before considering these causes in detail I annex two numerical statements, which display the frequency of the several causes of nephritis at different periods of life:—

Supposed Causes of Nephritis in 86 Children between the Ages of 2 and 12, from the Hospital for Sick Children.

Scarlatina	*75*
Measles	3
Cold	5
Erysipelas	1
Acute rheumatism	1 (?)
Eczema	1
	86

I have collected from my own notes 50 cases of nephritis in adults in which the causes appeared to be reasonably clear. The preponderating influence of cold is apparent. This agency, alone or with others, accounted for 30 of the 50.

Supposed Causes of Nephritis in 50 Adults (Ages from 20 to 53).

Exposure to cold or wet	23
Cold or wet together with drink	6
Drink	6
Scarlatina	7
Acute rheumatism	3 (?)
Malaria with exposure	1
Sleeping in newly-painted house	1
Pregnancy	1
Destruction of one kidney by tubercle	1
Heavy weight (sack of coals) falling on loins	1
	50

Some of the causes of nephritis may be considered in further detail. Cold in the adult is the most frequent of all the causes of the disease, definitely accounting for more than half of the cases. Among children cold is far less common in this relation than scarlatina. To produce the result the cold must be applied in a temperate or warm climate. Nephritis or renal dropsy is not a disease of the arctic regions. I suppose the active combustion required for the maintenance of vital heat consumes matters which in other circumstances might be thrown upon the kidneys to their detriment. The tropics afford no constant protection from nephritis, however generally infrequent are inflammatory affections of the kidney in these regions. I knew an instance where a young officer was immediately attacked with severe nephritis during hot weather in India, after getting wet through in a thunderstorm and afterwards long sitting in a cold bath. Cold to produce nephritis is usually long or repeatedly applied, often during perspiration, and often during exhaustion or in connection with alcoholic excess. The cold, to be effective in the manner in question, is usually applied for some hours, often for days or weeks. A walk of several hours in snow, a long drive in cold weather, a day's work in cold and wet, may be cited as examples, as also may be a shorter exposure, as in the case of a drunken man who refrigerated himself by swimming in the Thames. Protracted cold bathing, apart from alcoholism, was presented not only in the case of the officer I have just referred to. Sometimes repeated exposure, day after day, in the course of out-door occupations, has been assigned as the cause, and in other cases the disorder has come on as the result of habitual or long-continued exposure. A Cornish quarryman worked for six months under a cliff, which formed the side of the quarry, from which water dripped upon him, so that he was generally wet all day, and got home wet through in the evening, often not changing his clothes. This was followed by gradual loss of health, pains in the loins, and chronic œdema, with urine albuminous to three-fifths. I knew an officer in whom an attack, at last fatal, followed upon a month's exposure to cold and snow in Armenia. There are many instances in which the attack has declared itself, usually by facial dropsy, almost immediately after the exposure, as on the evening of the same day ; in other cases it has come on later and more insidiously. A very intense and rapidly fatal variety is apt to present itself in middle-aged drunkards who take cold in some accidental manner, perhaps connected with their vice.

The passing of bile with the urine is a definite cause of nephritis. The epithelial cells of the kidney become intensely yellow, and a tubal inflammation is set up, which imparts to the urine albumin and epithelial casts. Nephritis of this origin is temporary when the cause is so; it is seldom severe, and not usually productive of constitutional symptoms.

Diabetes also is apt to set up nephritis and make the urine albuminous. The irritating quality of the saccharine urine, which is seen in its action upon the mucous membrane with which it comes in contact, may be the reason; but I have sometimes asked myself whether both the albuminuria and the glycosuria may possibly have to do with the same cerebral irritation. Enough changes have been found in the brain of diabetes to indicate morbid action in it, though not enough to fix the seat or display the steps of the morbid process. It was long ago shown by Claude Bernard that while irritation of one part of the medulla made the urine saccharine, irritation of another part made it albuminous. It is conceivable that a morbid change may produce both results at the same time. But I will not dwell on speculative considerations. The albuminuria of diabetes is of the nature of nephritis. This condition is more serious and lasting than when due to the elimination of bile, but only in exceptional cases gives rise to marked constitutional symptoms. A great physician, no longer with us, used to say that a man had better have both albumin and sugar in the urine than one without the other. It is true that the albuminuria in these circumstances is not usually of a very active or mischievous kind. But I have seen cases in which, with marked diabetes, there has been equally marked renal disease, with albuminuria, dropsy and cardio-vascular changes, and in which it was difficult to determine which was the primary or which the more important disease. I have known albuminuria and glycosuria to concur apparently as the results of inheritance; or rather, glycosuria to present itself together with albuminuria in certain members of the family to which I have already alluded in which albuminuria was hereditary. The connection between the two conditions under such circumstances is not obvious.

With regard to the loss of one kidney as the cause of inflammation in the other, it has sometimes happened, though rarely, that after the destruction of one of these organs the other has been found to be in the large white state of chronic nephritis. It is not within my experience that acute renal inflammation has ever been attributed to this cause. It sometimes comes to pass, and need be noted as a source of error, that after the destruction of one kidney by a suppurative process the other is found to have become the subject of lardaceous disease, which in former times was not sufficiently distinguished from nephritis.

One of the most important causes of renal disease must be held to be scarlatina, whether we have regard to the frequency of the organic inflammation from this cause or to its too often enduring character. Unlike the nephritis of diphtheria, which is relatively more frequent, that of scarlatina is peculiarly apt to involve the Malpighian bodies and the interstitial tissue, and to leave lasting mischief. The different results of these two diseases suggest that in scarlatina the poison is especially discharged by, or has a special relation to the Malpighian vessel; while in diphtheria the part so selected is the epithelium. But so long as the scarlatinal poison itself is only a matter of hypothesis, speculations upon its demeanour are idle.

Not only does scarlatinal nephritis continually prove fatal as acute renal dropsy, but it is no uncommon experience to trace the chronic granular kidney to an attack of this fever many years before. In such a case it is possible that there may have been no early dropsy, even no dropsy at any time; though the broken health may with sufficient probability be followed back to the remote disorder of which the renal result was imperfectly evident in the recent stage. At the same time, it is to be fully recognised that a large proportion of attacks of scarlatinal nephritis pass off in the recent stage and leave no wrack behind. It is certainly the exception for a person, whatever his age, to pass through an attack of scarlatina without the presence of albumin in the urine; though there may be only a trace, and that for a short time, in which case there may be no other sign of renal disease. The late Dr. Hillier found albumin in about half the cases of scarlatina under his care at the Hospital for Sick Children; my own experience would fix the ratio higher, though it is to be recognised that the frequency of nephritis varies in different epidemics. [*Vide* art. "Scarlet Fever," vol. ii. p. 154.] How large a proportion of children who suffer from renal dropsy owe this to scarlatina will be apparent from the table at page 359, where it is shown that of 86 cases of nephritis, of which the causes were recognised, 75 were traced to this. Scarlatinal dropsy is rare under a year old, though I have known it at the age of ten weeks. The number of deaths from this affection,[1] as might be expected from the incidence of scarlatina, increases from the first year to the fourth, after which it steadily diminishes. Among grown people the proportion of dropsy, or nephritis, which presents itself as the result of scarlatina is comparatively small, though it is an item which has to be reckoned with. The table at page 359 shows that in the adult nephritis is attributed to scarlatina far less often than to cold, perhaps less often than to drink; though the intermixture of the alcoholic with other morbid influences makes it difficult to speak exactly.

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[1] See Dr. Tripe's table, deduced from the reports of the Registrar-General referred to in my book on *Albuminuria*.

Scarlatinal nephritis may come on at any period after the first appearance of the febrile symptoms. With malignant scarlet fever the urine is often bloody, scanty, and albuminous almost from the first. Where the fever is very mild, so as to be possibly unnoticed, the renal affection may be the first ostensible sign of illness; though in such a case inquiry will probably show that the child has been exposed to the infection, was afterwards feverish, and perhaps had a sore throat. According to Dr. Tripe, the dropsy most often appears on the fourteenth day, but may be delayed even to the eighth or ninth week. Dr. West assigns the second week of the disease as the most common time for the commencement of the renal sequels, and believes that if delayed later they are usually mild. Of 60 cases at the Hospital for Sick Children 5 showed dropsy within a week of the appearance of the rash. In 42 the dropsy began between the end of the first week and of the fourth; in the remaining 13 it came on in the second month; in 2 near the end of it. Speaking generally, the probability of renal mischief lessens much after the first month, but is not over until after the second. It is to be fairly inferred that the kidneys are among the selected *loci* of the scarlatinal poison, or are especially irritated by it as it makes its exit; but the state of the skin has also a bearing upon the renal manifestation. It is impossible to dissociate cutaneous desquamation from scarlatinal nephritis; the time of desquamation is especially that of nephritis. Exposure to cold particularly during this time is apt to bring it on, insomuch that in convalescence from scarlatina greater care is necessary in this respect than in the corresponding period of perhaps any other febrile affection. In the critical state of the scarlatinal kidney it is obviously inadvisable to throw upon it more than can be helped of what should escape by the skin. It was once the vogue to anoint the peeling surface with a mixture of olive oil and lard, by way of preventing the scattering of the scales which were thought to be the chief vehicles of infection. But it is to be doubted whether these are the chief agents in carrying the disease; and at any rate the stopping-up of the pores with grease cannot but further embarrass the cutaneous functions already impaired by the desquamating process. These considerations were suggested to me by observing, as I thought, a disproportionate amount of renal disease in patients so treated.

The next cause of nephritis which calls for especial mention is diphtheria. The albuminuria, or in other words the nephritis, of diphtheria differs from that of scarlatina in these important particulars; it is almost always present, it is early, and it is for the most part harmless. Albumin is so constantly found in the urine with diphtheria, and that so early, as to constitute a valuable indication as to the nature of the affection of the throat. The albuminuria is rather an accompaniment than a sequel. Dr. Hillier, at the Hospital for Sick Children, found the urine to be albuminous in all but five of thirty-eight cases of diphtheria; and in thirteen, where the urine was examined daily, there were seven in which it was found so before the fourth day of the disease. In the remaining six the advent of the albumin was between the fourth day and the nineteenth.

Lasting renal disease seldom ensues from this cause. If the patient recover from the diphtheria, so as a rule does he from the renal complication. I have known renal dropsy to be thus produced and even prove fatal, but such results are very infrequent. The nephritis appears to be chiefly tubal, as must be inferred from the abundance of epithelial and hyaline casts in the urine and the infrequency with which persistent disease is left behind.

The evidence of acute rheumatism as a cause of genuine or general nephritis needs to be carefully weighed. It is not unknown for blood, albumin, and casts to present themselves in the urine in the course of acute rheumatism, but it is to be borne in mind that renal embolism is a concomitant of rheumatic endocarditis, and may be the source of these additions. Renal embolism is not attended with dropsy, and cannot account for this symptom should it be present. But rheumatic endocarditis may give rise to dropsy, and also to renal congestion, which may make the urine bloody and albuminous, and thus simulate nephritis in so many particulars that the distinction is not always easy or possible. Be this as it may, I have known dropsy and albuminuria with the characters of nephritis to come on with, or closely upon, rheumatic fever and be attributed to it. But with the sources of mistake to which I have referred, and the obvious infrequency of rheumatic nephritis, if such a thing there be, I am rather sceptical as to the existence of any direct relation between the febrile and the inflammatory disease.

Alcohol, as a cause of renal disease, has given rise to some difference of opinion. Enormous, almost inconceivable quantities of alcoholic liquor are often taken without any such result. As a cause of the granular kidney alcohol occupies a very subordinate position. But with regard to nephritis, and that of a somewhat acute kind, we have evidence that the cause is by no means an infrequent one, though far less frequent than cold. I have already adverted to the efficacy in this respect of cold and alcohol acting together, but alcohol alone is efficient. A kept woman, aged twenty-eight, having been deserted by her protector, took to furious drinking. Brandy and gin were her liquors, a bottle of brandy a day her habit, and intoxication more or less continuous. After two months of this she became generally dropsical, with marked urinary evidences of nephritis. A soldier, aged thirty-eight, who had served in India, received £68 as his share of the Banda and Kirwee prize-money. This he spent in drink, in seven months. Porter was his liquor, three or four pots daily his ordinary limit, according to his own statement, while occasionally he had a "bellyful," which he explained as five or six pots. After five and a half months of this process renal dropsy set in, for which, about the time his money was exhausted, he became my patient in St. George's. I was consulted in regard to a young lady, I think of about the age of nineteen, who acquired renal dropsy, and I doubt not a hopeless white kidney, after a long course of port wine in company with a vinous and unwise grandfather. Alcohol as a cause of nephritis is generally somewhat acutely administered; the result is more apt to follow a definite period of great excess than more moderate and habitual indulgence.

It is not possible to do more than enumerate, and that incompletely, the other irritants foreign to the body, by which various degrees of nephritis are produced. Among these may be mentioned cantharides, turpentine, phosphorus, lead, arsenic, silver, and mercury. The resulting inflammation is often brief and characteristically tubal, as in the cases of cantharides and arsenic. With lead the disease early assumes an interstitial position and permanent character.

Symptoms.—The symptoms of nephritis present themselves with varying degrees of acuteness, sometimes abruptly, sometimes insidiously. To take, first, the more acute form, which is usually due to cold, the symptoms which first attract notice are facial œdema and scantiness of urine, which contains albumin and casts, and often blood.[1] These urinary changes, together with puffiness of the face, may appear within a few hours of the exposure or on the next day. There may be dull pain or sense of weight in the loins and a general feeling of illness, but there is no acute pain or active distress; the disease makes its own sedative. There is often vomiting in the beginning of the disease as well as in its course, and there is total want of appetite. There is sometimes at the beginning, especially when the disease is the result of cold, a certain amount of febrile action, with dryness of the skin, but rigors are exceptional, as also is a continued high temperature; though the temperature is often raised by the various complications which are apt to occur in the course of the disease. Hardness of the pulse and dropsy begin and continue together. A time may come, after the acute disease has become chronic, when with a further increase of vascular tension and the superaddition of hypertrophy of the heart the dropsy will lessen or cease; but I refer now only to the acute or recent condition. This is chiefly characterised by dropsy and the state of the urine, though there are many complications which will modify the course and shape the end of the disease. The dropsy, as œdema, is general and especially conspicuous in the face, legs, and loins, though not so extreme as it is apt to become in cases which run a slower course than those now under consideration. The urine may be reduced to two, three, or four ounces in the twenty-four hours, and, especially when the attack is due to cold, may be black with blood, and will deposit not only blood corpuscles, but multitudes of large casts containing blood, renal epithelium, and fibrinous matter. The secretion is, of course, albuminous beyond what the blood explains.

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[1] In my work on *Albuminuria* I have considered the causes of nephritis in more detail than is possible here.

Blood is not always present, for there is a rapidly fatal form of nephritis which sometimes follows scarlatina in which there is no blood, though much albumin and a great abundance of large casts, chiefly fibrinous, but containing also renal epithelium. In such a case the urine may be almost suppressed as if the tubes were sealed up with the exudation. It may be found in such a case that the glomeruli are affected as well as the tubes. The diminution of the urine affords a rough measure of the severity and danger of the case, and its increase one of the most important signs of improvement. The less urine the more dropsy is a general but not a constant rule, for it sometimes happens that, as in such a case as I have referred to, the urine may be almost suppressed and œdema absent or only in traces. In these circumstances I have witnessed much vomiting, exhaustion, and feebleness of pulse, want of arterial tension rather than excess of it, and have associated the absence of dropsy with this condition. The urgent vomiting gives notice of uræmic poisoning, and forewarning of head symptoms. Absence of blood from the urine is not a good sign; it is probable that the bleeding relieves the congested organ, and does good rather than harm. Such cases as I am now discussing tend to death by cerebral uræmia most often displayed by repeated epileptiform convulsions variously intermingled with degrees of coma; a condition of semi-coma being finally succeeded by nearly complete unconsciousness and stertor, though the unconsciousness is seldom so profound or the stertor so guttural as ensues upon cerebral hæmorrhage.

It is not possible to make a definite separation between the acute cases and the subacute or chronic. A scarlatinal case, to which I have already alluded, proved fatal on the fifth day after the appearance of the albumin. An intense attack from cold ended fatally on the nineteenth day after the exposure. A similar attack from the same cause recorded by Bright lasted three weeks, the fatal issue having been, as we may suspect, hastened by the depleting treatment which was inevitable in the year 1827. The more rapid cases gradually merge into the more protracted, which we have presently to consider. When death takes place in the acute stage the condition of the kidney presents several variations which are determined largely by the cause of the attack. The organ is always swollen, smooth, and congested, and the congestion more conspicuous in the cones than the cortex, where it is more or less masked by the inflammatory products which in this situation are the more abundant. The appearance varies according to the degree of congestion and the contents of the tubes. The most striking variety is the chocolate or coffee-coloured kidney, which drips with blood when cut, and belongs chiefly to the intensely congestive form of the disease which comes on most often from cold. When from scarlatina the cortex has a pale or parsnip-coloured basis, which shows through the blood which the organ abundantly contains and exudes. The injection may be so abundant and so fairly distributed as to give a general pink colour to the section.

When nephritis takes its slower and more ordinary course, but is nevertheless severe, the urine becomes less bloody, supposing it to have displayed blood at the outset, and it increases in amount, though not to its normal quantity. The urine sometimes increases to much beyond the normal amount. If this happens early in the disease, before renal fibrosis and secondary cardio-vascular changes are established, it is a good sign, part of the natural process of recovery; the kidneys are responding to the diuretic action of the retained excreta, and all promises well. But I am considering a case which promises ill. The most conspicuous symptoms are usually dropsy and anæmia.

The dropsy, as general dropsy, is as extreme as any we know; though possibly some local dropsies, such as hepatic ascites, may be more intense within their limits. The areolar tissue is the first part to become infiltrated, though the serous cavities soon become similarly occupied I have known the thighs and back to become so distended as to discharge large quantities of serum through visible ports in the skin. I have known the abdomen to become so stretched partly from peritoneal and partly from integumental fluid that the true skin gave way, leaving, when the patient recovered, which she happily did, a liberal pattern of scar-like exaggerations of the *linea alba* of pregnancy. I could give other instances where, under similar circumstances, the skin has been variously injured by distension. The dropsy sometimes includes conjunctival œdema, a striking but not a common complication. As parts of the general dropsy, fluid frequently collects in the peritoneum and pleuræ, less often and in relatively smaller quantity in the pericardium. These accumulations belong rather to the later than the earlier stages of the disease. Of all renal conditions that of nephritis with the large white kidney tends most to dropsy. The outflowing may to a certain extent relieve uræmia, but is a source of danger in itself. The hydrothorax causes dyspnœa, to which the ascites contributes; beside which erysipelatous inflammation is apt to ensue upon the excessive œdema, and various local evils—cellulitis and abscess—often follow upon the surgical measures employed to relieve it. The dropsy and the anæmia which goes with it give visible characters to the disease, the bloated pallor and the water-logged carcase.

Beside the dropsy, which is the most frequent and conspicuous symptom, the course of the disease is varied, and often concluded by intercurrent attacks of an inflammatory nature, especially such as affect the respiratory organs. Pneumonia, broncho-pneumonia, bronchitis, and pleurisy are common, especially in the earlier stages, and more in young subjects than old. These occur without any recognisable external cause, as if the products of the disease acted as irritants to the organs of respiration. In the majority of fatal cases one of these conditions assists to bring about the final result. Pericarditis sometimes occurs, but far less frequently than with the granular kidney. A condition of the larynx, which may probably be termed inflammatory œdema, sometimes presents itself. Laryngeal dyspnœa comes on somewhat suddenly with alteration or loss of voice. The mucous folds above the epiglottis are swollen and puffy, and the epiglottis may be felt with the finger to be thick and prominent. Should the case terminate fatally, a general submucous infiltration will be found above the true cords, involving the epiglottis and arytæno-epiglottidean folds. Croupy breathing is the most obvious sign of this condition, which not infrequently precedes and contributes to the fatal ending. I may here interpose a word to the effect that this complication is often successfully treated by liberal acupuncture of the parts affected and the inhalation of steam. Membranous inflammation of the larynx—true croup—has sometimes been known to occur under such circumstances as I am considering, especially in hospitals; but I think that this has been truly diphtheritic and the result of infection, not a simple result of the renal disease.

Uræmic attacks, usually convulsive in nephritis, frequently occur in the advanced stages of the disease, or in intense forms of it not of long standing. Epileptiform seizures present themselves, often, but not always, preceded by vomiting or headache; and may recur at short intervals and in great numbers, perhaps sixteen or seventeen in as many hours. The intervals are occupied by drowsiness or incomplete coma. The attacks are often fatal, but not necessarily so. When they occur in acute disease, in young persons, and when the kidneys are capable of recovery, they often pass off under treatment and leave the patient none the worse. To show the frequency of uræmic head symptoms under nephritis, and the preponderance among them of convulsive attacks, I may state that of 63 cases of nephritis under my care in which recovery took place, convulsions occurred in 5; coma without convulsions not at all. Of 57 fatal cases, convulsions occurred in 17; coma without convulsions in 2. Thus it appears that of 110 cases of nephritis, inclusively, convulsions occurred in 22; coma without convulsions in 2. Thus, speaking of nephritis in general, it appears that convulsions occur in one-fifth of the cases.[1]

Nephritis is usually attended from the first with an increase of arterial tension, and as a consequence with the cardio-vascular changes which ensue upon it, hypertrophy of the heart and thickening of the arteries; and in advanced cases the retinal alterations which belong to the same process. I have distinctly recognised hypertrophy of the heart as a result of nephritis of not more than six weeks' duration. I need not dwell on these changes at present, as they will receive fuller consideration in connection with the granular kidney. It is to be borne in mind that the kidney of nephritis is not divided from the granular kidney by any abrupt separation or essential difference in the pathological process by which the two are produced. One may pass into the other. The cardio-vascular changes are of the same nature in both, their establishment being chiefly a question of time. It may be mentioned in connection with the vascular changes that epistaxis sometimes occurs with nephritis, though not so frequently as with the granular kidney.

The **duration** of nephritis cannot be expressed in absolute terms. Of those who completely recover, the vast majority do so within a year. Of those who die, the majority do so within six months, though there is a small but very conspicuous minority in which the acute condition becomes chronic, and the chronic condition permanent, lasting in one shape or another for many years, possibly with a delusive interval of apparent health between the beginning and the end. I found that of 50 fatal cases of all ages the termination in all but one occurred within the first six months; but the whole story is not revealed by this comparatively limited record. There are many cases, particularly after scarlatina, when fibrosis is peculiarly apt to assert itself, where the later stages take the almost indefinite chronicity of the granular kidney, which is the organic condition ultimately attained to.

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[1] I have given further particulars in my book on *Albuminuria*, to which I have already referred.

The causes of death in nephritis vary according to age. Under sixteen the fatal issue, in more than half the cases, is brought about by some inflammatory affection of the organs of respiration. After sixteen this cause accounts for only about a seventh. Cerebral uræmia takes the second place before sixteen, and the first after that age. Dropsy and its direct consequences at both periods come next to uræmia, next to this, at both periods, peritonitis, and then pericarditis, which is very infrequent with nephritis as compared with the granular kidney.

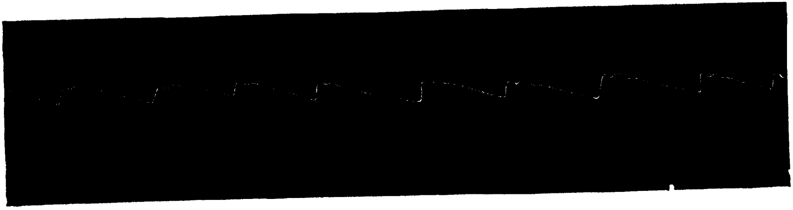

Fig. 1.—Pulse-tracing in acute nephritis of 14 days' standing in a boy aged 14. Marey's sphygmograph. 150 grammes pressure.

The urinary changes of nephritis may be briefly indicated; within the space to which I am limited it is impossible to do more. The urine is usually diminished in quantity at the outset, sometimes nearly to suppression; while during recovery, should this occur, it is often greatly in excess of the normal amount. It often, at the very beginning, gives traces with the guaiacum test of the blood crystalloids, while at an early period corpuscular blood generally presents itself, sometimes in large quantity. Much albumin is early present, which diminishes with the stress of the attack. Albuminuria with nephritis is so nearly constant that an exception has the interest of a curiosity. I will mention one. A male child of the age of ten months had what could not be otherwise regarded than as acute renal dropsy. There was no history of scarlatina or of other cause. When he came under notice the disorder had lasted a fortnight. There was then much general œdema, which became extreme until the eyes were nearly closed by the surrounding swelling, the limbs distended, tense, and shiny, and the hands and feet nearly globular.

After two convulsive attacks he died ten days after he was first seen. The water, which was extremely scanty, could be obtained only on one occasion. It was ammoniacal. There was a doubtful trace of opacity after heat and acid, leaving the presence of albumin equally a matter of doubt. The kidneys were buff-coloured and firm in texture; the pair weighed one ounce and half a drachm. The tubes were generally occupied, and in some places distended with epithelium and fibrinous cylinders. Prepared sections failed to display any interstitial change. The case was one of intense tubal nephritis.

Tube-casts of various kinds and renal epithelium seldom fail to show themselves in great profusion.

To revert in brief to one or two particulars: the diminution of urine at the outset furnishes a rough measure of the severity of the attack. I have often known the urine to be reduced to less than two ounces in the twenty-four hours, and occasionally to about half an ounce. Such diminution is generally a fatal omen. It is generally dependent either on nearly universal stoppage of the tubes or the extensive participation of the Malpighian bodies in the inflammatory process. Diminution to a less extent, for example to half or a quarter of the normal amount, is continually followed by recovery, this process being often attended with diuresis. I knew an instance in which this salutary flow amounted to 240 ounces in twenty-four hours. The specific gravity gives an average of about 1019; in the most acute conditions, where the secretion is very scanty, the specific gravity may be much higher; in the later stages it is often as low as 1010, or even lower. In the early stages, and sometimes for long afterwards, the urine may be black with blood, or it may present only an almost invisible trace, or none. The total absence of blood, particularly in an acute case, is not a good sign, but the reverse; the hæmorrhage appears to relieve the organ. Epithelial cells, sometimes fatty in the later stages, are usually found. Early in the disease these may be so abundant as to form a sediment conspicuous to the naked eye. Casts of the tubes are generally present, the abundance of which is usually commensurate with the activity of the disease. The special cast of recent tubal nephritis is the epithelial, a delicate cylinder of fibrin embedding epithelial cells. Sometimes the cells are so massed together that nothing else is visible. Blood appears in the casts, or may even chiefly compose them during the hæmorrhagic process. In the advanced stages of the disease the tubes sometimes lose their epithelial lining, and discharge casts of large diameter and strongly-marked outline, consisting chiefly or entirely of transparent fibrin. During recovery the casts diminish and ultimately disappear.

There is a condition to which the term acute nephritis applies, though the inflammation appears to be limited to the interstitial tissue; with this there may be little urine, much albumin, acute and general dropsy, and all the constitutional symptoms of ordinary diffuse nephritis, such as results in the large white kidney; but with all these evidences of acute renal inflammation there may be no casts from first to last. Such cases [illegible]e rare, and, so far as I have seen, fatal. They may be described by the term acute interstitial nephritis.

It may suffice to give a brief summary of the chemical changes in the urine in nephritis. Albumin is almost always present, sometimes in amounts which are greater than are found in any other renal disease. The maximum is about 35 grammes, or an ounce and a quarter in twenty-four hours. The loss of even half this amount would probably tell, by way of impoverishment, upon the system at large. All the normal constituents are diminished—the water, the urea, and the chlorides—to a greater extent than occurs in any other disease of the renal substance. The phosphoric, sulphuric, and uric acids are reduced in a less marked manner; of these, the uric acid apparently suffers least. In some cases, indeed, during the process of recovery, uric acid is discharged in abnormal abundance; and a similar statement may be made with regard to the urea and the water.

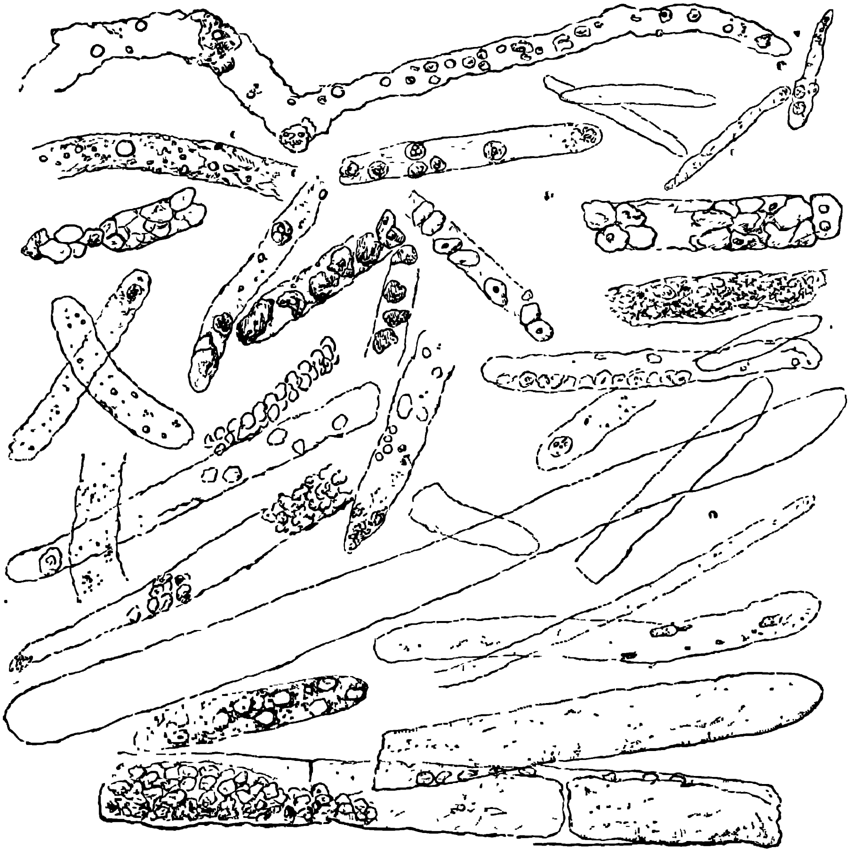

FIG. 2.—Casts of nephritis containing fibrin, epithelial cells and granular matter One large cast includes others in its interior. (From Dickinson's *Albuminuria*.)

Treatment.—In treating nephritis we may generally hope that we have to do with a disease which has a natural tendency to get well, so that our endeavours must be not so much to cure the patient, as to place him in favourable circumstances for recovery. Certain complications may, however, present themselves in which active interference is called for. The primary considerations which must guide our conduct are these—to abate renal hyperæmia, and to avoid whatever may produce it in the shape of renal irritants; to relieve the kidneys of work so far as is consistent with maintaining an abundant flow through the tubes; to ensure this flow, without irritating the gland, so as to keep the tubes clear; to keep the skin active and the bowels free, and thus direct into other channels matters which might otherwise be thrown upon the kidneys to the injury of these disabled glands. The keeping down of uræmic accumulation is a secondary though important purpose which the measures indicated will subserve. The diet in an acute and recent case should be wholly liquid or only with the admission of a little farinaceous food. Arrowroot may be commended as both liquid and farinaceous, but more solid foods of this class may be given in the early progress of the disease. Milk may be given freely, but the diet should not wholly consist of it. Light animal broths should be included; no concentrated essences, but thin beef-tea or thin broth of other kinds. It is essential that water should be freely introduced, either pure or sophisticated. Lemonade and barley water serve the purpose, but perhaps pure water is best of all, especially distilled water, such as may be obtained under the name of Salutaris. Malvern water is nearly equally pure and is more palatable. Water, whether pure or only slightly modified, is the best of diuretics; not only is it without irritating properties, but it lessens by dilution any irritating quality which the urine may possess. Alcohol should be entirely inhibited unless there be some special reason for its employment. The patient should be kept in a warm bed in a warm room, at a temperature not high enough for discomfort, but higher than is common in a hospital ward or sick chamber. Hot-air baths may be called for by any threatening of uræmia, but are not generally necessary. It is essential that free action of the bowels should be ensured. I am accustomed to begin with a mercurial purge, calomel with compound jalap powder or haustus sennæ, and to follow it up with a saline laxative. Sulphate of magnesia is perhaps the best purgative in such cases as I have in view, while one of the alkalising salts of potash should be in some way superadded. We must not forget that sulphate of magnesia is decomposed by the vegetable salts and carbonates of the alkalies. A small dose, 2 or 3 drachms, of the sulphate may be given every morning, and a drachm of potassio-tartrate of soda, or of tartrate or citrate of potash, three or four times a day. A drachm or half a drachm of sulphate of magnesia may be given in an ounce and a half of water, together with a drachm of tartrate of potash; the solution decomposes, but does not at once precipitate. After a time iron becomes desirable. In the later stages I have been in the habit of giving at bed-time and on rising some such mixture as this—

a drachm of sulphate of magnesia, a drachm of aloes wine, and ten minims of the tincture of perchloride of iron. If it be desired to include an alkalising salt, tartrate of potash may be given with tartrate of iron and a little decoction of aloes. Digitalis must receive especial mention as demanded whenever the urine is very scanty, as it usually is in the early stages, and when dropsy is present. This invaluable remedy may be introduced as infusion or tincture into any of the mixtures which I have mentioned.

Some of the complications require special treatment, others none. The horizontal posture must be strictly maintained when the legs are affected, which is usually the case. The paramount effect of digitalis has already been adverted to. If other measures are needed, periodical hot-air baths, best to the legs only, are of great service; they not only remove the fluid, but by purifying the blood they correct the condition on which the dropsy essentially depends. Hydragogue purgatives at regular intervals are of service for similar reasons, but neither sweating nor purging must be too energetically enforced, since they may injuriously increase the anæmia which is one of the factors of dropsical effusion. Puncture of the legs should be avoided when possible on account of the local inflammations which are apt to ensue, and are often fatal. Antiseptic precautions should be strictly employed, notwithstanding the apparently trivial nature of the operation. The belly may be tapped with less danger, and generally with advantage, and with relief to the legs as well as to the abdomen. I have often thought especial and general relief to follow from tapping one of the pleuræ when it contains much fluid; not only does this relieve the breathing, but by taking pressure off the lung it releases the general venous outlet and promotes absorption. Uræmic convulsions, or the threatenings of them, must be met promptly and vigorously with eliminants, hot-air baths, and hydragogue purgatives. The hot-air bath may be up to the neck, if the circumstances are pressing; and if it fail to produce free sweating, the patient may be immersed for two or three minutes in a bath of very hot water, say 108°, and the hot air again applied. If the blood-pressure be high and regular, the hot air may be preceded by a subcutaneous injection of pilocarpin; but this dangerous dosing must be used with great caution, and at the initial dose should not be more than one-tenth of a grain. Of purgatives, elaterium is the most effective; calomel is also of use, combined with some quick aperient, and may generally be given with safety if not repeated. Should the convulsions be violent and alarming, chloroform, chloral, or bromide of potassium may be used as a palliative, though it is with some unwillingness that one poison is thus added to another. Inflammatory attacks must be treated on general principles with a general avoidance of opium and mercury. Œdema of the glottis usually yields to the inhalation of steam and acupuncture. Pericarditis is little under the influence of medicine.

When the disorder has assumed a chronic and quiescent form it is necessary, among other precautions, to guard against anæmia. The rigidity of diet may be relaxed, and a little meat and fish allowed, perhaps one meal of each daily. Iron is generally called for, which, as a rule, should be associated with some laxative so as to ensure two actions of the bowels a day, or three in two days. Other medicines being now put aside, it will suffice to give morning and night, or in the morning only, such a mixture as I have already referred to, containing iron, sulphate of magnesia, and aloes, the doses being adjusted to produce the desired effect. In the later stages of chronicity a resort to a warm climate, especially in winter, may be of great service.

II. THE GRANULAR KIDNEY.—**Pathology.**—The pathology of the granular kidney may first receive attention. The essential alteration is an overgrowth of the interstitial intertubular or fibroid tissue as the result of a slow process akin to inflammation, or amounting to it in its most chronic form. The overgrowth is succeeded by contraction and the compression of the tubes and Malpighian bodies to their gradual atrophy and partial extinction. The morbid change is analogous to that which in the liver leads to cirrhosis. There are two modes by which the contractile renal fibrosis which eventuates in the granular kidney may be produced, which, however different in their beginning, are virtually the same in their results. Most frequently the granular kidney comes on insidiously, with no early symptoms, by way of chronic and long unnoticeable change in the interstitial tissue. Less often the mischief is set going by an acute attack of diffuse nephritis, such as follows scarlatina, or may be due to other causes.

The granular kidney of gradual origin may be traced in its pathological progress by putting together post-mortem observations relating to different stages. In this condition the intertubular overgrowth is of gradual production and in small amount; the contractile process follows closely in the wake of the hypertrophic, so that the organ shrinks from the first. The contractile overgrowth shows itself as a fine hypernucleation which begins under the capsule and about the blood-vessels, and works its way inwards so as to involve in time the greater part of the cortical tissue. The hypernucleation usually presents itself in wedge-shaped regions, with the base at the surface, the apex pointing inwards, and slowly extends to the intermediate and deeper parts. The tubes are separated, variously constricted, and in places practically destroyed, though remnants may be discovered with the microscope. The Malpighian bodies surrounded with new contractile tissue are in like manner compressed and sometimes obliterated.

The naked-eye changes are at first slight, the capsule becomes thickened and adherent, the surface loses its smoothness and its even curve, and becomes beset with small projections which are but faintly indicated, and which look like exaggerations of the minute subdivisions into which the surface is normally subdivided by the blood-vessels. The projections are not actual outgrowths, but are made by the drawing in of the intergranular intervals by the contractile process. The separating vessels are often enlarged and somewhat stellate. The colour on surface and section is as yet little altered, or may be of a somewhat deeper tint than natural. In time the superficial granulations become more declared; the cortex first, then the whole organ, shrinks and cysts are developed, notwithstanding which there is much loss of bulk, so that ultimately the weight of the organ may be reduced to half what it was. In the advanced stages the superficial granulations are often large, pale, and conspicuous, and sharply contrasted with the vascular depressions which lie between them. They are more or less hemispherical, or at least present the shape of segments of spheres. The cortical layer between the cones and the capsule may now be no thicker than a shilling, while the deeper parts are also reduced in bulk, the cortex more than the cones. The general colour of the organ on surface and in section may be more or less buff, or it may retain much of the reddish or brick dust colour with which it started. In a practical outline of this kind it is needless to follow the minute changes in detail. The leading factor is the development of the intertubular contractile growth, to the strangulation of the essential elements of the gland. Large regions of the tubular structure are virtually destroyed, the tubes being reduced to attenuated and useless remnants, or even entirely replaced by fibrous tissue. The epithelium is variously atrophied, compressed, and distorted by the contractile process. The Malpighian bodies resist longer than the tubes, and sometimes groups of them may be seen close together or in absolute contact, all the intervening structures having disappeared while these only remain. In time many of the Malpighian bodies are destroyed, or reduced to a small size by compression. Sometimes they undergo a cystic transformation as a result of the obstruction of the tubes with which they are connected; fluid collects between the capsule and the vessel, with dilatation of the one and compression of the other. Together with the tubes the intertubular capillaries are obliterated or rendered impervious, and thus an obstacle is put in the way of the escape of the blood from the surviving Malpighian bodies. This cannot fail to enhance the blood-pressure in the Malpighian coil, and thus increase the watery discharge from it, a consideration which may help to explain the polyuria of the granular kidney. The arteries, large and small, are thickened. The primary renal arteries are measurably thickened in both their coats, but their calibre is not considerably or constantly diminished. I have taken some pains to ascertain the point by measuring with the *rota meter*, with the help of enlarged outlines, the internal circumference of the renal artery in granular and healthy kidneys. I find that though the artery of the granular kidney is more various in size than that of health (2), yet that the average calibre of the two is practically the same; I found it to be exactly the same in the male, nearly the same in the female. This point has its interest as concerns the renal circulation. Many years ago I ascertained, by directing water through the renal vessels, that the granular kidney on an average (18) transmitted less than a quarter of the amount transmitted by the healthy kidney under corresponding circumstances. Thus it seems that there is a great obstruction in the renal circulation, and that this is not in the large arteries. It must be placed in the minute vessels of the gland, the arterioles of which are visibly thickened and narrowed, while it is obvious that the capillaries are extensively destroyed.

Small cysts are very often found in the cortical tissue of the granular kidney and displayed upon the surface. These are made out of the tubes which are cut into segments by the contractile tissue outside them. An occasional but not a necessary change in the kidney of this kind, as of that of nephritis, is a general fatty degeneration of the epithelium.

This sketch of the morbid anatomy of the granular kidney of gradual and concealed origin will serve in most of the later respects for that which comes on as the sequel of acute nephritis. But the early stages are different, and to them a few words of separate description must be given unless this outline is to be left conspicuously incomplete. The large white kidney of nephritis is usually fatal as such, with the kidney large and smooth, or only with a few dimpled depressions to indicate the beginning of contraction in the still excessive bulk. It must not be forgotten that with the large white kidney the inflammation involves not only the tubes but the interstitial tissue, which with time and opportunity may take upon itself the contractile process which is the essential agent in the making of the granular kidney. When nephritis proceeds to granulation it may be presumed that the inflammation is protracted rather than intense, and that the large white stage, though more or less accomplished, has not been as fully declared as when death has been its immediate result. The granular kidney of this origin, though it may have become smaller, even much smaller than natural, still retains on surface and section much of the pale or parsnip tint which belongs to nephritis. The shrinking is most marked under the surface ; the retention of the nephritic character is most conspicuous in the deeper parts between the cones, which are often compressed in their centres to the well-known wheat-sheaf shape. The longer the disease lasts the more the characters approximate to the ordinary type of the granular kidney, so that after a time it may be difficult to decide whether the disorder have been of chronic or acute origin.

For clinical purposes the granular contracting kidney, putting aside that of lardaceous disease, may be dealt with as one and indivisible, without any attempt to distinguish the symptoms according to the origin of the disease, whether in chronic change or as the result of nephritis.

Sex and Age.—As to the subjects of the granular kidney, *sex* may be considered first. It would be easy to multiply evidence on this head, but it may suffice to say that of 250 cases collected from the post-mortem books of St. George's Hospital, 165 related to male, 85 to female subjects, and that this proportion of two to one is found generally to apply. It is obvious that some of the causes of this condition, notably lead and gout, affect males more often than females. This may partly, but probably does not wholly, account for the difference.

The age at which the disease proves fatal, or of which evidence is found after death, ranges, according to my experience, from 5 years to 82, and no doubt wider information would extend the limit in both directions. It is rare before 20, but I could mention cases fatal at the respective ages of 5, 10, 11, 12, and 14, and many between 14 and 20. The following statement compiled from the post-mortem books of St. George's Hospital gives the age at which death took place in 242 instances:—

Age.	Deaths.
0 to 20	1
21 ,, 30	17
31 ,, 40	38
41 ,, 50	73
51 ,, 60	55
61 ,, 70	43
Over 70	15
	242

Causes.—The frequently obscure origin of the disease invites a particular inquiry into its *antecedents*. Of these the following are ascertained as causes of the granular kidney, or at least have to be considered in relation to its origin:—

i. Climate, whether predisposing or exciting, but at any rate exerting an overruling influence with regard to the origin of the disease. ii. Long precedent acute nephritis, or scarlatina possibly without ostensible nephritis. iii. Gout. iv. Lead. v. Alcohol. vi. Valvular disease of the heart. vii. Pregnancy. viii. Malarial fever. ix. Obstructions to the exit of urine. x. As part of general fibrosis. xi. Heredity. xii. Mental depression.

I will now proceed to consider some of these causes in detail. The overruling influence of climate cannot be dealt with here, excepting in general terms. I may refer for particulars to the chapter on "Climate in Relation to Renal Disease" in my work on *Albuminuria*. For the present purpose it may suffice to say that the disease in question prevails most in the temperate zone; that it is more common in England, Holland, Germany, and the Northern States of America, than in the South of France, Italy, the islands of the Mediterranean, and places still farther to the south. Coming to causes of less general and more definite application, the first consideration must be given to *antecedent acute nephritis* as a cause of the granular condition; not that this is a frequent cause in comparison with others, but it forms a link of connection between the subject of the present section and that of the preceding. In old days there was much dispute whether the granular contracted kidney was a sequel of the large white or was of independent origin. The fact is that both modes of origin occur, the independent frequently, the consequential infrequently. Scarlatinal nephritis is especially apt to involve the interstitial tissue, and to be succeeded, as has been already stated, by granular contraction. A boy died in St. George's Hospital under the care of Dr. Ogle. He had had scarlatina severely three years previously, and never been well since. He manifested the symptoms of the granular kidney in a marked manner, and after his death displayed the pathological appearances with equal distinctness. A woman died under my care at the age of twenty-one of chronic albuminuria, which was apparently continuous with an attack of scarlatinal dropsy eleven years previously. The immediate cause of death was pericarditis. The kidneys, which weighed together but three ounces, were characteristic examples of the granular and fibrotic. A boy, of the age of fifteen when last seen, was frequently under my care in St. George's Hospital with chronic albuminuria traceable to scarlatina seven years before. His heart was hypertrophied, and no doubt his kidneys granular. I lost sight of a young woman at the age of sixteen in a similar condition, which was apparently the result of scarlatina at the age of three. The granular kidney may be a late result of scarlatinal dropsy, or, as there is reason to believe, it may be a remote sequel of scarlatina without the intervention of dropsy, or of any of the outward and visible signs of acute nephritis. When chronic renal disease follows acute renal dropsy the dropsy disappears as the heart hypertrophies, so that in the ultimate stages dropsy may be only a matter of history.

Gout, *Lead*, and *Alcohol* are so intermixed as causes of disease that they may be conveniently taken together. The granular kidney is so commonly associated with gout that the "gouty kidney" has become another name for the granular. It is evident that the gouty disorder precedes the renal, and may be presumed to be the cause of it. Gout is one of the results of chronic lead poisoning, which toxic condition may cause the granular kidney either together with gout or independently of it. Given the lead, it may be said without fear of over-statement that no other cause of the granular kidney is as efficacious, though as only a minority of the population are subjected to the influence of this powerful poison, other causes taken together may produce the result more numerously. Of 45 men who died in St. George's Hospital with granular degeneration, 10 had been concerned with lead in the way of trade. Of 42 workers in lead who died from disease or accident in the same institution, 26 were found after death to have granular kidneys—in other words, the painter or plumber, be his end what it may, is more likely than not by the time he has reached it to have acquired this organic impairment. Lead is known to be excreted by the kidneys, and it is probable that the morbid action of this metal is as a renal irritant. This usually acts slowly with the result of the granular kidney, though instances occur less frequently in which acute nephritis is produced by the same cause. Alcohol is a renal irritant of less effect than lead. Some alcoholic liquors, notably beer and wines, the sugar of which is not completely exhausted by fermentation, cause gout, of which the gouty kidney may be a part; but, on the whole, alcoholic drinks have a less influence in causing renal disease than has often been supposed. The kidneys and the liver are very differently circumstanced as regards drink. The liver receives it from the stomach at first hand; as much as survives hepatic action has to be passed through the lungs before it can reach the kidneys. Much of this volatile substance must be got rid of by evaporation and expiration, so that the proportion which remains for renal elimination must be small. Alcohol has indeed been recovered from the urine by distillation, but only in small quantities and when much has been taken; and it may be believed that of the amount introduced into the stomach the proportion which reaches the remote renal exit is under ordinary circumstances insignificant. A drunken debauch, as has been previously stated, is capable of causing acute nephritis. There is a large, smooth, somewhat congested kidney, partly tubal and partly interstitial, which is begotten of beer, upon the persons chiefly of draymen; and alcohol in general has at least some influence in causing granular contraction. The activity of this cause may be roughly measured by a comparison which I formerly instituted between the kidneys of persons whose employment made them conversant with liquor (draymen, potmen, and the like), and those of others who had no such association.[1] Of 149 persons to whom drink was presented in the way of duty, 31 were found after death to have granular kidneys; of the same number of persons to whose occupations drink bore no relation, 27 displayed granular kidneys. The difference is less than would have been presented had alcohol any such overpowering influence upon the kidney as it has upon the liver. I may mention by way of illustration that in the same series cirrhosis of the liver was found in 22 of those employed about liquor, in only 8 of those employed otherwise. As bearing upon the exaggerated views which have been taken with regard to the effects of alcohol upon the kidneys, it may be stated that persons who have died with delirium tremens present no larger proportion of kidney disease than persons who have owed their death to accident without any such complication. In the course of thirty-one years at St. George's Hospital 58 post-mortems were made after delirium tremens. In 28 the kidneys were healthy, in 15 congested, in 7 granular or cysted. In the same number of examinations after death from accident, without delirium tremens, the kidneys were found to be healthy in 24, congested in 7, granular or cysted in 15. Delirium tremens may be accepted as a proof of alcoholism, but before drawing conclusions it must be stated that the average age at death after delirium tremens was thirty-eight, after death without it forty-one. We may at least infer that such an alcoholic habit as suffices to produce delirium tremens does not do so much to make the kidneys granular as three years of additional life.

Valvular disease of the heart and disease of the kidney are often found together. The relation is a double one; each may cause the other under circumstances which will presently appear. Cardiac hypertrophy dilatation and consequent mitral regurgitation are consequences of renal disease, particularly of the granular kind. Mitral regurgitation from this cause is a late and not very frequent consequence, but nevertheless is a very real one. The mitral disease, for such it must be called, consists only of dilatation without any morbid change in the flaps, but it is enough to give rise to murmur and all the clinical resuls of mitral regurgitation. The evidence that the granular kidney is sometimes a cause of endocarditis may be accepted, but for practical purposes it need not be greatly regarded. On the other hand, there is evidence in abundant detail that valvular, especially mitral disease habitually causes renal change which may proceed to the granular kidney. Habitual venous congestion of a solid organ—the liver, the spleen, or the kidney—causes induration of its substance. As a result of valvular imperfection particularly mitral, general venous congestion is produced and maintained. As regards the kidneys, they become full of blood, red, hard, and somewhat increased in size; the capsules adhere more firmly than natural, and after a time the surfaces become finely granular and give evidence of contraction, while cysts sometimes present themselves in the cortical tissue. An early change, as revealed by the microscope, is accumulation of epithelium in the cortical tubes; increase of the interstitial tissue and fibrosis occur later, and are of slow and scanty development as compared with what takes place when the renal disease is of different origin. Though fibroid thickening and hypernucleation are superadded in process of time in a considerable proportion of cases of prolonged mechanical congestion, I have often failed to find them even when the peculiar hardness of tissue has led me to expect them. In the course of five years I made post-mortem examinations of 153 persons with valvular disease; 29 of these had the kidneys hard, congested, and increased in bulk, but still smooth, 67 had granular surfaces and contracted cortices. Thus valvular disease is frequently a cause of renal, and it may be added that renal disease of the granular kind is sometimes a cause of valvular; not only by way of dilatation of the orifice, as has been already stated, but occasionally by setting up endocarditis.

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[1] See notes at end of chapter.

When albuminuria and mitral regurgitation concur, as they often do, the inexperienced may doubt which is the primary disorder and which should give the chief direction to the treatment. What is to be determined is whether the albuminuria is due to independent renal disease or to congestion of cardiac origin. In advanced cases of renal disease, where the cardio-vascular changes are conspicuous and the heart greatly enlarged, it is probable that the regurgitation is brought about by the disease of the kidney; but more often, when cardiac and renal symptoms present themselves together, the cardiac is primary, the renal secondary. The distinction is of great practical importance, for if the albuminuria is merely the result of mechanical congestion, it will be got rid of or made better by treatment directed to the heart. The results of digitalis and mercury in such a case are often such that the physician is glad to make a diagnosis which suggests their employment. On the whole, the kidneys are tolerant of the congestion of heart disease. Persistent change is slow to establish itself. The urine, after being albuminous, may, under treatment, cease to be so. Uræmia seldom declares itself. Dropsy, when present, is more cardiac than renal.

Far otherwise is it with *pregnancy* as a cause of renal disease. Here, as with heart disease, we recognise mechanical venous obstruction, but whether because it is applied in a manner especially injurious to the kidney, or because it is conjoined with other circumstances which are so, it is apparent that the puerperal state is one of the most active causes of renal disease to which woman is subjected.

It has long been known that in a considerable proportion of cases the urine is albuminous during the later months of pregnancy, a condition which may be merely transient, or may eventuate in lasting renal disease. The urine usually becomes albuminous in the later months, after the fœtus has attained a considerable size, and moved from the pelvic to the abdominal cavity. It is obvious that this change of position and increase of bulk must be attended with compression of the vena cava, and possibly also of the renal veins, and it is a matter of observation as well as of inference that congestion of the kidneys is a consequence. In many cases the mechanical nature of this process is shown by the limitation of the œdema to the lower extremities, and the absence of constitutional symptoms of renal disease. In other cases the constitutional results declare themselves; the face becomes dropsical, dropsy indeed may become more or less general; and, together with other renal symptoms, there is frequently that variety of uræmic convulsion which from its circumstances is known as puerperal. There has been some difference of opinion as to the immediate cause of the disorder of the kidney which ensues upon pregnancy. The probability is that the cause is complex or at least duplex. Mechanical congestion is a certain factor, but there is in all likelihood something more. The kidney, as has been already shown, is tolerant of mechanical congestion which is slow to produce active disease. The kidney disease of pregnancy is far more actively mischievous than that of heart disease, it more rapidly takes on serious organic change, and quickly gives rise to renal consequences.

The changes which occur in the kidney as consequences of pregnancy may be briefly indicated. They are the changes of heart disease and something more. To passive congestion is superadded an active inflammatory process. In an early stage there is much hyperæmia with obvious fulness of vessels, general redness, and some increase of size. In a case destined to further trouble, a somewhat peculiar form of diffuse nephritis succeeds; the tubes become loaded with epithelium, which early takes on fatty change and imparts a yellowish colour in streaks or otherwise to the section. The fatty change is not limited to the epithelium, but may be somewhat general. The tubal change is accompanied or quickly followed by interstitial nucleated contractile growth, with consequent compression of the tubes, particularly near the surface, and superficial granulation. The condition is one of general nephritis, upon which granular contraction ensues with inordinate rapidity. So early does the contractile process become superadded to or intermixed with that of inflammatory swelling, that the more bulky results of renal inflammation are excluded; the large white kidney does not, under these circumstances, present itself. The early access of inflammatory change would seem to imply that other causes are at work beside the mechanical, and that these are analogous to those to which other forms of nephritis have been traced. It has been suggested that the kidneys are irritated by some product of pregnancy, possibly an excrementitious result of fœtal nutrition. The conjunction of the two morbid agencies, the mechanical and the vital, may account for the greater activity of the disease as compared with the granular kidney of other origin.

I think I have observed that women of slender frame more often contract renal disease under pregnancy than those of more liberal outline. The mischief usually presents itself in the first pregnancy, at the end of which it may prove fatal by way of puerperal convulsions. Should this not happen, the renal symptoms rapidly become mitigated after delivery, to be aggravated with every recurrence of pregnancy. The disorder, unless re-initiated by repetition of the cause, may long remain quiescent, or even undergo slow improvement. It by no means follows that, because the urine be albuminous and the legs dropsical, permanent disease will result; these may be simply mechanical; if, however, the face be also swollen, we must infer enough renal change to produce constitutional results, and regard the condition as one of gravity. Although, in this place, I am dealing only with the causes of disease, not with its results, I may conveniently interpose a few words of more general bearing. The puerperal kidney has a mixed nature; it is one of diffuse nephritis, upon which granular contraction is rapidly superimposed; the nephritic character is early evinced by dropsy, which may be widely spread and even extreme; the results which more especially belong to the granular state are declared later, but are even exaggerated as compared with the common consequences of this condition when it is of other than puerperal origin. The tendency to acquire the retinal and other secondary lesions appears to be disproportionately great. As to treatment, prevention is the great desideratum. If a first pregnancy has declared the danger, it is much to be desired that there should be no recurrence of it. When it is ordered otherwise, and renal symptoms become pressing, the induction of premature labour may be an absolute necessity, the only measure which is capable of affording the relief needed.

Malarial fever, especially of tropical origin, is frequently succeeded by persistent or chronic albuminuria, which we need have no hesitation in associating with the granular contracting kidney. I have frequently recognised this condition in persons who have returned from India after having suffered repeatedly from the effects of malaria. It is probable that the disorder is brought about by the recurrent attacks of intense congestion, to which the kidney, together with other abdominal organs, notably the spleen and the liver, is subjected under the malarial influence. As complicating and intensifying this influence is the fact that the same malignant agency is a frequent cause of hæmoglobinuria, or "intermittent hæmaturia" as it is also termed; and that this is capable of acting locally upon the kidney as a cause of nephritis and probably of its remote sequels. Most of the cases of renal disease of presumed malarial origin which I have seen have been in returned Indians. The symptoms have been such as to indicate the fibrotic kidney, mostly very chronic or quiescent, and comparatively harmless. There has been little or no tendency to dropsy, more to the cardio-vascular change. A distinguished Indian medical officer, who had seen much service, and suffered long and severely from malarial fever, returned to England in the year 1872 with urine albuminous to a third, and some indications of cardio-vascular change. The albumin diminished with occasional periods of increase, and at last ceased to be constantly present. He has led a very active life since his return, and is now (1896) in the enjoyment of good health, excepting that he is slightly gouty, and that the urine sometimes displays albumin.

I call to mind two instances which ended fatally with renal symptoms. One of these did so after sixteen years in England, most of which were spent in active professional work. The disorder long remained without apparent progress, but ultimately was succeeded by uræmic asthma and convulsions. In neither of the cases mentioned was a post-mortem examination practicable.

Obstruction to the exit of urine, or the irritation which some cause of obstruction has set up, is sometimes to be traced among the antecedents of renal fibrosis. The liver occasionally becomes fibrotic or cirrhotic, in consequence of obstruction by gall-stones, and the kidney appears to suffer in a similar manner from a similar cause. Two of the most marked and pathologically complete cases of the granular kidney which I ever witnessed in early life—they proved fatal at the respective ages of twelve and fourteen—gave evidence at death that the escape of urine from the kidneys had at some bygone time been hindered. In the younger there was dilatation of one kidney and of the other ureter; the elder had been operated on for stone at the age of three, and after death one kidney was found to be dilated and atrophied. More or less fibrosis of the kidney, together with glandular atrophy, is indeed not seldom to be recognised as a consequence of long-standing retention of urine. It is probable that this irritating fluid, probably made more so by ammoniacal decomposition, being detained at high pressure in the renal cavities, soaks into and irritates the renal structure and sets up inflammatory action.

The granular or fibrotic kidney has been thought to be but a part of a *general or cardio-vascular fibrosis*, and herein lay the contention of Gull and Sutton which it is not needful in this place to follow in detail. It must be allowed that with age, alcohol, and possibly other circumstances, the arteries deteriorate and the fibrous skeletons of the solid organs increase at the expense of their more actively vital constituents; but it is not necessary to reiterate, what has been abundantly shown, that the granular change in the kidney is chiefly produced by causes which act especially, and in the first instance, upon this organ and not indifferently upon the body as a whole. The granular kidney frequently succeeds upon inflammation limited to the organ. It often presents itself at an age so early that it is impossible to credit the arteries with any general deterioration or fibrosis unless it be the result of the renal mischief. And there is ample clinical evidence that the cardio-vascular change associated with the renal is, as a rule, not a contemporary and parallel alteration, but is subsequent to that in the kidney and presumably produced by it. That the renal fibrosis, of which a granular surface is the outward expression, is local to the kidney and not general to the body is shown, as I have elsewhere insisted, by the pathological independence of the liver and kidney. Cirrhosis of the liver and granulation of the kidney have little tendency to occur together. I found that in 250 cases of the granular kidney the liver was cirrhotic but in 37, or 1 in 7. Valvular disease may act conjointly on both organs, and produce a lesser degree of fibroid thickening in both: alcohol may thus affect the liver much and the kidneys a little; but the rule is that each of these organs is acted on by morbid causes proper to itself, and not shared by the others or common to the whole body.

The heredity of the granular kidney stands on the same basis as that of the chronic form of diffuse nephritis, of which it is a sequel (see *Nephritis*, p. 357).

It has been thought that the form of renal disease under consideration is sometimes consequent upon mental depression. There appears to be a double relationship in this respect; advanced renal disease of this nature is sometimes attended with lachrymose depression, and there are instances in which this disease has come in so immediately upon depressing circumstances that it may be conjectured to owe its origin to them (Allbutt). Mental disquietude is a diuretic of no mean efficacy, and it may possibly be a cause of organic renal change. If it be so, the relation is by no means singular; cancer and tubercle are both invited by mental distress.[1]

Finally, there are many cases of granular degeneration, probably the majority, without ostensible cause, or only the tendency of race, or the influence of climate.

Symptoms.—In describing the symptoms of granular degeneration I will briefly indicate the common course of the disease, and then touch upon its deviations. The ordinary form is that which begins gradually and insidiously, not that which succeeds upon acute nephritis. The patient, commonly a man between forty and sixty, loses his health by such imperceptible degrees that it is usually impossible to say when the disease began, or what was its cause. If gout or lead is in the record the cause is ready to hand, otherwise it is likely to be doubtful. The earliest obvious indications are usually hardness of the pulse or slight œdema, perhaps amounting only to puffiness. The urine is now discovered to be albuminous, though perhaps only to a trace; the heart is found to be hypertrophied, and the conclusion is obvious, not only that the kidneys are diseased, but that they have been so for a considerable time. Dropsy may be totally absent for long or altogether, particularly if the heart be much hypertrophied and little dilated. The cardio-vascular changes, together probably with some alteration in complexion and aspect, may even for a long course of years be the only outward signs of the disease. The patient, or rather the affected person, for he may not as yet be a patient, acquires a dirty pallor, perhaps something of puffiness, or sometimes a blotchy look such as is associated with free living. The urine will probably be pale and superabundant, will be passed with some frequency, especially at night, and will display albumin,—very little at first, perhaps only a trace, afterwards more; especially when in progress of time the interstitial change becomes complicated with tubal. With this the urine lessens in amount, and some degree of dropsy usually presents itself, though not to the extent which characterises nephritis of acute origin. Pain in the back in the renal region is occasionally present, but more often not. It is, however, sometimes severe, and made worse by shaking. When this has been so, it has happened to me to observe after death an unusual amount of adhesion about the capsule and cellular tissue.

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[1] See paper by Professor Clifford Allbutt, *Brit. Med. Journal*, Feb. 10, 1897.

Sometimes dropsy is absent from first to last. Occasionally there is a good deal in the later stages, especially when the hypertrophied heart has become dilated so as to permit of regurgitation through the mitral orifice. This may be accompanied with a definite mitral murmur, though the valve-flaps may be perfectly healthy. In such a case there may be pulmonary apoplexy with hæmoptysis, and the dropsy may take many of the characters of that of cardiac origin, which indeed it partly is, become considerable and general, and affect not only the legs, but the pleuræ and peritoneum.

Various symptoms may intervene during the progress of the disease, and possibly some of them may have been the first means of calling attention to it. Among these are vomiting and various forms of dyspepsia. The vomiting is no doubt generally excited by the secretion of uræmic matter into the stomach. It occurs independently of food, often in the morning before breakfast, and results in the production of a little slimy matter, which often has an alkaline reaction. When the renal disease is associated with the special form of ulceration of the bowel which, as I have shown, goes with it, then is the vomiting most urgent. I have known it to be habitually provoked in such a case by the sound of the dinner-bell. Vomiting is more characteristic of the granular kidney than is diarrhœa, which in my experience is rare in this connection, more so than constipation. Before the differentiation of lardaceous disease diarrhœa was somewhat generally attributed to albuminuric affections; but without being quite unknown in other conditions, it is the especial accompaniment of the lardaceous form. Among other symptoms are headache, dimness of vision, and asthmatic attacks. Hæmorrhages of various kinds occur more particularly when the heart has become hypertrophied and the arteries deteriorated. Epistaxis is not infrequent, and may be obstinate. Cerebral hæmorrhage has its association with the granular kidney, though when it occurs it is more often found that the kidneys are slightly than extremely affected. Of all hæmorrhagic affections, that of the retinæ, which will be presently dealt with separately, is the most frequent, and diagnostically the most significant. More fatal and less obvious is the albuminuric ulceration of the bowel which is of hæmorrhagic origin. To this I shall revert presently; I have already mentioned hæmoptysis as a late result of the granular kidney. Other evils beset the long course of the disease before it reaches what may be considered its normal ending in cerebral uræmia. Many inflammatory affections occur; bronchitis is exceedingly common, pneumonia and pleurisy are frequent, peritonitis occasional (vol. iii. p. 635). Pericarditis is frequent; it comes on insidiously, often without noticeable symptoms, and is almost invariably fatal. It is not unusual for it to remain undiscovered until after death. The brain participates, though perhaps less than might be supposed, until it is violently overcome by the uræmic poison. The patient sometimes becomes lachrymose, sometimes restless and irritable; and occasionally, especially in the advanced stages, there is transient delirium or temporary mental failure with delusion. These are bad signs. The idle comments foretell the ending of mortality. Among the later and less frequent complications is a scaly skin disease—a form of dermatitis.

This formidable catalogue of possibilities must not be allowed to give too discouraging a prospect. Many or most of them may never be encountered, the patient may pursue the even tenor of his way almost undisturbed by his disease, and may live almost indefinitely, fairly useful and reasonably comfortable. The disease for many years may give no sign of its presence excepting to the medical observer, and to him only by the albumin in the urine and the changes in the heart and vessels.

Though the foregoing outline is intended to relate to the disease of gradual development, a few words will suffice to make it apply equally to the kind which succeeds upon acute nephritis. The granular kidney sometimes declares itself years after an attack of scarlatina, as in cases to which I have already referred. Sometimes the later affection is in obvious continuity with scarlatinal nephritis, shown by œdema and albuminuria, or possibly the connection of the renal disease with the exanthem may be indicated only by an intermediate period of indefinite bad health. Nephritis of other than scarlatinal origin may be similarly followed, though with more infrequency. As the acute disease becomes chronic the heart enlarges and the dropsy disappears. It is an instructive fact, as bearing on the direct causation of the cardio-vascular changes by the renal, that these consequent alterations attain their most typical development in young persons, often children, in whom the renal fibrosis is an obvious result of acute inflammation. The granular condition having been fully attained, it matters little whether the beginnings were in chronic change or acute disease; the symptoms and issues in the later stages are what have been already indicated.

The **duration** of the granular kidney is difficult to limit, since the beginning is usually unrecognisable. In hospital practice the disorder does not come under notice until it has reached an advanced stage and manifests the symptoms which belong to it. From private sources it would not be difficult to collect cases which have endured for ten or twenty years. I know a gouty gentleman who enjoys fair health at the age of seventy-two, whose urine has been albuminous for fifteen years. He has much cardiac hypertrophy, and has had hæmoptysis, no doubt of renal origin. That he is a subject of the granular kidney is beyond doubt. On the other hand, instances occur, though rarely, in which the renal fibrosis takes an acute form with symptoms resembling in most respects those of tubal or diffuse nephritis. I will subjoin an instance of what might be called acute interstitial disease of the nature of fibrosis, though scarcely amounting to it.

A married lady, aged forty-four, whom I saw frequently with Dr. Buzzard, furnished an example of this form of disease. She had had several children, the last five years before her attack. She had never had any dropsical symptoms with her pregnancies; there was no record of gout, no history of scarlatina, or exposure to cold, or of anything else which could be assigned as the cause of her disease. The beginning was sudden. She was perfectly well, as far as was known, until one day early in October 1894 the feet were found to be greatly swollen, and in three or four days, without any feeling of illness, the whole of the lower extremities were œdematous. The urine was then found to be highly albuminous. Throughout the subsequent course of the illness it remained so, and was generally much reduced in quantity. The urine never contained blood; no casts nor any other morbid deposit were found. I examined the urine on many occasions with the result that casts were uniformly absent. The dropsy increased upon the limbs, and invaded the peritoneum and pleuræ; acupuncture of the legs and paracentesis of the abdomen were repeatedly called for. The skin assumed in its most characteristic form the ivory pallor of renal dropsy. Vomiting was latterly a distressing symptom, and there were two or three convulsive uræmic attacks. Towards the close the dropsy spontaneously diminished, until at last little remained. Death was brought about by gradual loss of strength connected with the inability to take or retain food. She died on 9th October 1895, her illness having lasted almost exactly a year. Her mother, it is stated, died of dropsy supposed to have been of renal origin. I am indebted to Dr. Colman for the account of the post-mortem, and also for some sections which I examined as well as himself. Both kidneys were in much the same condition; small, hard, slightly granular on the surface, and with adherent capsules. The cortices were much diminished. The renal arteries were atheromatous; the left renal vein contained a firm, old thrombus, which however did not completely obstruct the channel. Under the microscope the chief morbid appearance was universal, and profuse hypernucleation of the interstitial tissue, by which its bulk was notably increased and the tubes often widely separated. The increase was of young nucleated material rather than of old fibrous tissue. The Malpighian bodies showed nothing special. A large number of the tubes were natural, some contained plugs of amorphous substance.

Secondary changes.—The foregoing outline of the course of the disease may be filled in with a somewhat more particular account of one or two of its more important consequences, pathological and clinical. The comprehensive change in the heart and arteries must receive the first consideration as common to the whole body and to almost every case. It has its physiological and its pathological aspect, its uses as well as its disadvantages; it obviates some of the symptoms and causes others. It will suffice for the present purpose to describe briefly the *damages in the circulating system which occur in connection with the granular kidney*, and to refer also with brevity to the clinical consequences which follow upon them. I shall avoid as much as possible matters in dispute, but shall deal chiefly with simple observations and practical issues. It has already been shown that the changes of which I am about to write are not confined to the kidney which has acquired or attained to the condition of granular contraction (see p. 367), but are manifested as the same in kind if less in degree, as the results of nephritis upon which granulation has not yet ensued. As the renal changes advance, so do the cardio-vascular, until the incipient changes of nephritis pass into the general hypertrophic thickening which goes with the granular and contracted kidney.

Taking a well-marked instance of the granular kidney, the following changes are to be recognised in the circulatory system. The heart and the arteries together become hypertrophied; the heart in both ventricles, and the arteries in both muscular and fibrous coats, and of every size. The hypertrophy of the heart is nearly invariable with the granular kidney, but not quite. I have estimated that, not including cases where pericarditis is superadded, in which cases renal hypertrophy of the heart may be reckoned as almost surely present and often extreme, this cardiac change occurs in a decided form in 74 per cent of the fatal cases of the granular kidney. If cases with pericarditis had been included, the percentage would have been larger. It is, indeed, exceedingly rare to find this form of renal disease without some evidence of the associated cardiac change. But, however infrequently, cases do occur in which the cardiac complication (salutary adjustment it may be called) is absent, and it has been observed that they pursue a more unfavourable course than when it is present.

The heart displays the hypertrophy most obviously in the left ventricle, but the right shares in the same process. The weight of the heart may be doubled or trebled. I may mention incidentally that when the hypertrophy is extreme, pericarditis is very apt to occur as the finishing stroke. I have before me a series of thirty-one cases illustrating the cardio-vascular changes of renal disease; in nine of these the heart and pericardium together weighed between 20 and 39 ounces. The heaviest without pericarditis or pericardium weighed 23 ounces. In addition to hypertrophy the left ventricle in course of time often dilates, with the result of insufficiency of the mitral valve and all the results which follow this lesion; mitral murmur, increase of dropsy, pulmonary apoplexy. The dilatation marks the beginning of the end. So long as the heart holds its own, the hypertrophy appears to be beneficial. Under its influence, or at least together with it, it is continually found that the dropsy, if there have been any, diminishes and often entirely subsides, to reappear, as I have said, when the heart gives way; the last form of dropsy being worse than the first. How the beneficial action is brought about may be open to discussion, but one way seems clear. The ventricle has a double action; it not only drives but it draws. By its expansion it must tend to suck the blood out of the lungs, and thus clear the way for the emptying of the veins and relieve the venous circulation. It is manifest that this suction power, probably not very important in health, must be greatly enhanced by thickening of the ventricular walls, particularly when their stiffness is not impaired by increase of the cavity.

The systemic arteries, as has been stated, are thickened throughout their whole course from the heart to the capillaries, and it is to be inferred from the hypertrophy of the right ventricle that the pulmonary arteries are similarly affected, though probably to a less degree; with regard to these vessels, however, observations are wanting. The systemic arteries, more especially those of smaller size, are thickened both in their muscular and fibrous coats, and Gull and Sutton believed that they found a thickening also in the capillaries, not of course muscular, where no muscle is, but what they termed hyaline. As to the arteries, there is no doubt as to the general thickening of their walls, and as to both muscular and fibrous coats being thus affected. I need not detail observations which are accessible elsewhere; but I may briefly say that I have ascertained that not only are the arterioles thus changed, but also, though to a less extent, the larger arteries—to wit, the aorta, the innominate, the common femoral and the renal. The changes are therefore universal to the systemic arteries. The hypertrophy of the arterioles is often succeeded by fatty degeneration, which affects chiefly the muscular coat but is not confined to it. Sometimes small vessels are seen which are so disorganised by fatty change that little else can be made out. This is most often seen in the pia mater, probably because the vessels in these situations are more easily examined than elsewhere. The arteries are thus weakened, while the force brought to bear upon them by the ventricle is increased, a combination which explains the frequency of hæmorrhage under the circumstances.

The *clinical signs of the cardio-arterial changes* have become well known, and need not here be discussed at any length or in technical detail. From the outset of nephritis, before any increase in the size of the heart is recognisable, the pulse is hard to the touch, and gives evidence under the sphygmograph of increased pressure. This implies some difficulty in the emptying of the arteries, which is the cause of their over-tension, and ultimately of the thickening of their walls and of the ventricular hypertrophy. Taking a case of long standing, where the granular contraction of the kidney is well marked, the pulse changes are more pronounced. Two alterations are now to be discerned—increase of tension and thickening of the artery, both contributing to increase the hardness of the pulse. The educated finger, or I should say fingers, are as instructive as the sphygmograph, or even more so. The artery is usually large and permanently tight, the difference between systole and diastole only to be appreciated by firm pressure. If a finger be lightly passed across the vessel it will feel like a cord which knows no variations of size; and it will be found abnormally difficult to stop the current in it; it may even be that this cannot be done by any amount of pressure which can conveniently be brought to bear upon it. To judge of the force or "stopability" of the pulse it is best to use two fingers and both hands in feeling it, make pressure on the vessel with one hand, and with the other estimate the stream which emerges. It may be found that a pulsation of thread-like smallness will pass in spite of almost any pressure which the finger can apply. The sphygmograph gives similar evidence, and enables the increased force of the pulse to be accurately measured.

As to the heart, the signs of hypertrophy scarcely need to be dwelt upon. These chiefly relate to the left ventricle, the apex beat being displaced downwards and outwards, even to the extent of an inch outside and two inches below the nipple. Occasionally, though the heart is greatly enlarged, the apex beat is so distributed as to be scarcely perceptible owing to the rounding of the lower end of the organ. The first sound is muffled and prolonged; it may be nearly indistinguishable owing to the thickness of the muscular wall through which it has to come. Cases of this sort furnish a convincing proof that the first sound is made in the interior of the heart and not within the wall; it is intracardiac and not muscular; were it muscular it would be increased, not diminished, by the thickness of the muscle. Beside the signs of hypertrophy are those of intra-arterial tension, one of which is accentuation of the second sounds. It is to be noted that, contrary to what might perhaps have been expected, the pulmonary second sound is more accentuated than the aortic. Accentuation of these sounds is due to the increased blood-pressure in the great vessels. There is also under the same circumstances, but by no means constantly, a reduplication of the first sound, or some approach to it, which indicates a want of synchronism between the ventricles.

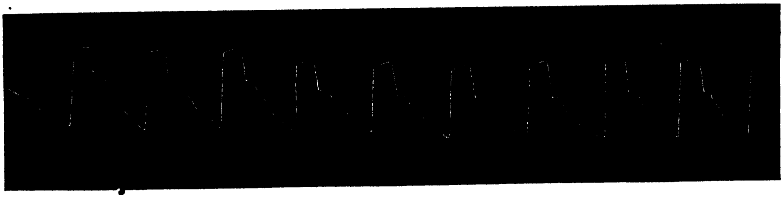

FIG. 3.—Pulse-tracing in a case of granular kidney in a painter aged 65. Marey's sphygmograph. 150 grammes pressure.

The damages in the circulatory system which have been indicated are manifested clinically by many hæmorrhagic accidents, which give its leading character to the disease, and are more vitally important than anything in its course excepting the uræmia with which it normally terminates. Some of these accidents have not yet been noticed; others require more notice than they have yet received. Pulmonary apoplexy and hæmoptysis of renal origin need not be further dwelt upon, nor is it needful further to mention epistaxis. With regard to apoplexy of the brain, the frequency of renal disease as a concomitant has been already referred to. Of 75 persons who were examined at St. George's Hospital after death from intracranial extravasation, 31 were described as having kidneys in a decided state of granular degeneration. This enumeration does not include slight degrees of renal change, which were numerous. Under this association cerebral apoplexy has been known to occur at an age to which it does not commonly belong. I have elsewhere related the case of a girl who died at the age of twelve with an extravasation in the brain as large as a goose's egg. The kidneys were in an extreme condition of fibrotic disease; the heart was hypertrophied to the weight of 8½ ounces, and the arteries were characteristically thickened and affected with fatty degeneration. That the arterioles should often give way under the circumstances which have been described is no marvel; while the vessels are weakened the heart is strengthened, intra-arterial pressure is increased, while the power to resist it is diminished.

Next to the brain in position, and perhaps in importance, comes the retina. With regard to this I gladly avail myself of the special knowledge of Mr. Brudenell Carter, who has undertaken this subdivision of the subject, and who writes as follows:—"The frequent occurrence of impaired vision during the progress of 'dropsy' has been known to physicians from a very early period; and Dr. Bright, when conducting the researches by which he connected 'dropsy' with disease of the kidney, was not unmindful of the fact. In an article on renal dropsy, which he contributed to the volume of Guy's Hospital Reports for 1836, he mentions, in the introductory portion, dimness or failure of sight as a common symptom or complication; and he also mentions it specifically as having been present in some of the instances which he describes; although, in an appended tabular account of 100 fatal cases, the principal post-mortem appearances in which are set forth with some fulness, neither the state of the vision nor the presence of morbid changes in the eyes is referred to. The eyes, indeed, do not seem to have been examined in any of these cases; and the impairment of sight received only a small degree of attention, probably because, at that time and for some years afterwards, it was regarded as a conspicuous example of alteration of nervous function, due to the nerve being supplied with 'imperfectly depurated blood.' In 1850, Türck discovered, by post-mortem examination, that the retinæ of a patient who had died from renal dropsy were studded with spots of fatty degeneration. A similar condition was afterwards found by Virchow and others; and, in 1856, Heymann published the first account of the ophthalmoscopic appearances which have since become so familiar. The issue, in 1863, of Liebreich's *Atlas der Ophthalmoscopie* carried the matter a step farther, and rendered a highly-coloured picture of what he described as 'retinitis albuminurica' accessible to many physicians who had not yet learned to use the ophthalmoscope for themselves. The characteristic feature of this form of 'retinitis' was said to be the presence of a group of white spots, arranged in a conspicuous stellate figure around the macula lutea; while other spots of the same general appearance, but usually larger and more isolated, and often accompanied by patches of effused blood, were irregularly distributed over the fundus. This particular combination of appearances, or even the presence of the stellate figure alone, was long thought to be pathognomonic of kidney disease; but more extended experience has shown not only that the stellate figure may be absent in renal cases, but also that it may be present in cases which are not renal. In 1872, for example, a young woman who might have sat for Liebreich's picture of 'retinitis albuminurica' was admitted into St. George's Hospital, and died there, with healthy kidneys, of tumour in the cerebellum. A boy was admitted into the same hospital, at about the same time, with typical 'choked discs,' but with no stellate figures, no scattered patches, and no hæmorrhages, whose eyes led many highly-skilled observers, including several members of the International Ophthalmological Congress, then assembled in London, to form the opinion that he was the subject of an intracranial tumour. He died of pleurisy supervening upon advanced kidney disease, and no primary brain lesion was discovered by the most careful examination. A case similar to the former had previously been described by H. Schmidt and Wegner; and a few others of both kinds have since been recorded. Notwithstanding these, however, it is incontestable that a combination of hæmorrhages and of white patches in the retina, either with or without the central stellate figure, will, in the great majority of instances, indicate the presence of renal disease with a very near approach to certainty.

"As soon as the ophthalmoscopic examination of renal patients became general and systematic, it was discovered, as might have been expected, that the typical albuminuric retina represented an advanced stage of changes which were recognisable at a much earlier period, and which commence, in some cases, by the appearance of small and scattered white spots, in others by the occurrence of minute effusions of blood. In the experience of the writer, bleeding has been the more common initial phenomenon; and it has usually been first observed on the temporal side of the nerve, between the disc and the macula. The first hæmorrhagic patches are almost invariably seated in the fibre layer, and the distribution of the effused blood is governed by the anatomical conditions of the tissue. The blood makes its way among and between the nerve fibres, which are often visible in front of it as a delicate white striation; while the general outline of the patch assumes a brush-like or flame-like character. As the case proceeds, fresh bleedings occur in parts of the retina more remote from the centre, and white patches of varying outline and magnitude are formed in increasing numbers. In the majority of instances the optic disc itself, and the unaffected portions of retina, for a long time preserve nearly their normal aspects; while, in others, the disc may become swollen, its margin obscured, and the portions of retina between the spots and the blood patches dimmed and cloudy, as if from the presence of albuminous fluid in the meshes of the tissue. If we disregard minute anatomy, and consider the retina as a structure roughly divisible into two layers, an anterior and a posterior, the former of which derives its nourishment from the arteria centralis, and the latter from the vessels of the choroid, we may ascertain, even by the ophthalmoscope, that the changes associated with albuminuria are, as a rule, almost confined to the former. Sometimes, however, the choroidal circulation becomes implicated in the general disturbance, and then some displacement of the retinal pigment, and a greater degree of impairment of vision than is usual, are liable to occur.

"The general application of the word 'retinitis' to the changes seen in albuminuria has led many persons to conjecture that these changes must always be ushered in by some increase of blood-supply to the affected parts; and hence a preliminary stage of 'hyperæmia' has more than once been described. It is exceedingly difficult to ascertain the presence of 'hyperæmia' of the fundus oculi, the conditions of its blood-supply being liable to vary within rather wide limits; and, in the opinion of the writer, the changes are essentially degenerative, and only assume certain sub-inflammatory characters in comparatively rare cases, possibly as a result of the disturbance of tissue by the effusion of blood or by the deposit of fat. The latter occurs as an infiltration with fat cells, which are found most abundantly in the granular and intergranular layers of the retina, but which, in advanced cases, extend into the fibre layer also Aggregations of these fat cells constitute the white patches; in which, moreover, the nerve fibres are often found to be swollen, and to be studded with irregular nodosities.

"The presence of the characteristic retinal changes does not afford any indication of the nature of the kidney disease, or of the stage which it has reached. These changes are found in every malady which is attended by albuminuria; not only in 'Bright's disease,' but also, for example, in the albuminuria of pregnancy or of diphtheria, or in that consecutive to scarlatina. The retinal changes, in the experience of the writer, never precede the albuminuria; but, in Bright's disease, it is quite common for them to give rise to the first symptoms which direct attention to the kidneys. Both in hospital and in private practice patients who consider themselves in good health will seek advice on account of impairment of vision, and an examination of their retinæ will at once suggest an examination of their urine. On the other hand, cases of albuminuria are met with in which the retinæ remain unaffected to the last.

"Apart from the obvious indication to treat the eyes indulgently, and to protect them from attempts at overwork or from other manifestly injurious influences, the treatment of albuminuric retinal degeneration resolves itself into that of the affection upon which the albuminuria depends.. In the cases which depend upon diphtheria, upon scarlet fever, or upon pregnancy, it is not uncommon for the retinæ to clear up, and for normal vision to be restored, as one part of the process of general recovery. In the cases of chronic kidney disease from which no recovery can be expected, the impairment of vision usually increases with the increasing amount and area of degeneration, but it seldom leads to complete blindness."

Analogous to the retinal changes, connected as they are with hæmorrhage, are some which affect the bowel, and produce a special and fatal form of ulceration which, like the change in the retina, is essentially albuminuric. I have elsewhere fully described and exemplified this condition, to which I drew attention in the Croonian Lectures for 1876. I will therefore now content myself with referring to it somewhat cursorily. Under advanced renal fibrosis, together with its cardio-vascular accompaniment, submucous hæmorrhages are apt to occur in many parts of the alimentary canal, in the stomach rarely, in the intestines frequently, more particularly about the ileo-cæcal region. This is succeeded by a form of ulceration which often leads to peritonitis, perforation, and death (vol. iii. p. 962). The ulcers are small, circumscribed, and sharply cut; they are usually few or even solitary. They are not connected with any of the glandular structures of the bowel, nor do they resemble the ulcers of typhoid or tubercle, or of any other sort, except to a certain extent those due to fæcal irritation. Evidences of hæmorrhage are usually to be seen in their neighbourhood, and it is apparent that submucous extravasation is the process to which they owe their existence. The usual symptoms are diarrhœa, griping, abdominal tenderness, vomiting, and finally those of perforation.[1]

The hæmorrhagic tendency shows itself in places other than have been mentioned. Epistaxis is very frequent; sometimes it occurs comparatively early in the disease, in the later stages it is apt to be profuse and alarming. Menorrhagia is not uncommon. Hæmatemesis occurred three times in 68 fatal cases. Purpura and bleeding from the mucous membrane of the mouth are late and infrequent, but genuine renal issues.

Next to hæmorrhages, among the results of the form of renal disease under consideration may be placed inflammation. Of these, bronchitis is the most common, occurring in over a third of the cases. Pneumonia and pleurisy are about equally frequent, much less so than bronchitis. Next to bronchitis in frequency comes pericarditis, which was found in a recent state after death in 16 of 68 cases. This complication is more frequent with the granular kidney than with any other kind, and is almost invariably fatal, though often latent. There is usually no accompanying endocarditis, though endocarditis with or without pericarditis is to be recognised as an occasional result of the same renal condition. In the

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[1] Since this was in type I have learned that the concurrence of intestinal ulceration with renal disease has not entirely escaped notice, though I believe that I may claim to have been the first to point out the nature of the connection. Wilks and Moxon, in the second edition of their *Pathology*, 1875, speak of duodenal ulcers as, like gastric ulcers, due to the acids of the stomach, and, like gastric ulcers, often associated with Bright's disease; they also refer to diphtheritic colitis as met with together with a similar inflammation of the stomach and with Bright's disease. I have ventured to regard the intestinal lesion as specially connected with the renal, and that by way of cardio-vascular change.

68 post-mortem cases already referred to, recent endocarditis was observed in 4. Erysipelatous inflammation or cellulitis sometimes occurs, particularly as an attendant of dropsy; but is less common than with nephritis. Other eruptions of an inflammatory nature have been noticed in connection with Bright's disease, which I venture to refer to in this place, though they do not all especially belong to the granular kidney or that of interstitial nephritis. I have seen a marked form of eczema, together with nephritis, in course of recovery. Dr. Pye Smith has given quite a catalogue of eruptions which are apt to occur with renal disease. One of them has been termed *erythema leve*, and others described as roseolous or papular. A severe form of dermatitis has, during recent years, been added to the catalogue of renal inflammations, and is particularly associated with the granular kidney. The eruption first appears as a sort of erythema; vivid red blotches, which rapidly become papular, present themselves on the extensor surfaces of the limbs, and afterwards on the palms, soles, and face. The mucous membranes are at the same time affected, as is evident by soreness and congestion of the throat, and sometimes by inflammation of the auditory meatus. The cutaneous papulæ rapidly become confluent, and may be succeeded by various degrees and admixtures of desquamation, eczema, and pustulation. These eruptions are attended with much itching and irritation. They occur late in the course of the granular kidney, are preceded by evidences of uræmia, and are usually followed by a fatal issue. Dr. Le Cronier Lancaster, to whom we are indebted for an early, if not the earliest notice of this condition, while house physician to St. George's Hospital, collected eight cases of this kind; one was followed by recovery, seven by death. Post-mortem examination was made in six, in five of which the kidneys were granular, in one lardaceous. One of the cases in this series was that of a man aged twenty-five, who was a patient of mine. He had albumin to a sixth, much hypertrophy of the heart, and increased arterial tension, vomiting, diarrhœa, headache, and bronchitis; no dropsy. A reddish, elevated, papular eruption appeared on the man's legs and body, and afterwards on the face, which was accompanied with a burning sensation together with much itching. He had also red, smooth, tender patches on the throat, running at the nose and eyes, and discharge from the ears, both of which were swollen. The eruption became scaly, then pustular, and several superficial abscesses formed on the limbs, broke, and discharged fœtid pus. He died forty-one days after the appearance of the rash. The kidneys were found to be in a marked condition of granular contraction, weighing together only six ounces. The usually fatal issue of the condition leaves little hope for treatment, but I would venture a suggestion in this view. The presumed cause, saturation of the skin by uræmic products, seems to indicate a simple measure which, in the only case in which I have as yet employed it, was highly successful. I would suggest long soaking of the body in a bath of water at blood-heat, say 98° or thereabouts, which could scarcely fail to dissolve out much that it would be desirable to get rid of. This might be preceded by a brief immersion

in a weak solution of bicarbonate of potash, which would appeal especially to the uric acid, if, as is likely, this takes part in the morbid process.

Supposing the patient with interstitial nephritis to have escaped all the pitfalls by the way, his course will terminate in cerebral uræmia, which may be said to be the normal ending of his disease. It is obvious that as the kidneys fail in eliminating various constituents of the urine, these must remain behind unless they are expelled by other channels. The kidneys may fail in many ways as regards their excretory function. Obstructive suppression may forbid the exit of the urine as a whole after it has been completely formed by the kidneys, or at least while the kidneys are structurally able to form it completely. With Bright's disease the urine is not arrested, but rather is not formed, or formed only imperfectly. These differences of morbid procedure are attended with different results; the uræmia of obstructive suppression is different in many respects from that produced by disease of the renal substance. And with regard to diseases of the renal substance, differences are to be observed both in the impairment of the urine and the uræmic results which ensue. With acute nephritis it is common to find both water and solids diminished; with the granular kidney it is often found that while the solids are diminished the water is increased. The blood must therefore be differently affected in the two cases, and the results are not quite the same. Coma occurs in both. With nephritis there is generally convulsion; with the granular condition convulsion is often, but not always absent.

Uræmia.—Before proceeding to the consideration of the uræmia of the granular kidney, I will briefly discuss the nature of uræmia in a somewhat general sense. The chief function of the kidneys is to separate from the blood certain matters already existent in it in the form in which they are excreted. The chief constituent of the urine, the urea, appears not to be made by the kidney as the bile is by the liver, but to be simply removed by the kidney after having been made elsewhere. With regard to uric acid, there is some uncertainty as to its place of origin, whether renal or extra-renal. Whether any excrementitious compounds are constructed by the kidney as well as expelled by it is not known; but it would seem improbable that so complicated an epithelial arrangement as exists in the kidney should not be constructive as well as selective. Whether the renal exit be obstructed, or the kidney itself diseased, urea accumulates in the blood, and probably the same is true with regard to uric acid. But the question of uræmia is not limited to these simple considerations; it is complicated, and we must admit that it is but partially understood. What we require is examination of the blood under a variety of circumstances and in further detail than has yet been accomplished. It may be presumed that the blood in renal disease varies inversely as the urine; thus what the urine wants the blood abounds in, and conversely. The blood is deficient in albumin; it contains a notable quantity of urea and uric acid, and, according to some pathologists, ammonia; it holds an excess of mineral salts, probably of many as yet indeterminate matters, and generally of water. With regard, first, to the toxic effect of urea, this is now known to be less than was formerly supposed. It may be introduced into the stomach or veins of animals with little result excepting increase of urine. When the kidneys, from disease, are unable to respond, the case may be different. A large amount of urea is known to accumulate in the blood as a consequence of obstructive suppression, but the attendant symptoms are not those which ensue upon disease of the renal substance With obstructive suppression there is heart failure, some degree of somnolence, some degree of muscular twitching, but not general convulsion or coma. To produce these, something different from urea, or something in addition to it, is presumably necessary. The blood has been thought to contain ammonium carbonate due to the decomposition of urea, and the symptoms of uræmia have been attributed to this salt. In advanced kidney disease ammonia can be detected in the breath in more than normal quantity, and convulsions have been found to follow the injection of the ammonium salt into the veins of animals. But it has been objected that the free exhalation of ammonia which occurs with expiration must make it difficult for this volatile substance to accumulate in the blood. As somewhat contrary to the ammonia theory the alkalinity of uræmic blood has sometimes been found to be diminished, and importance has been attached to this deficiency. Much has been attributed to the toxic effect of retained potash salts, and food and physic regulated so as not to introduce them in large amount. Hydræmia has been thought to play an essential part in the morbid process. This condition is no doubt generally present, though Dr. Carter has shown that after fatal uræmia the brain substance contains a no larger percentage of water than in health. Hydræmia may be confidently put aside as playing no necessary, though possibly it takes a subsidiary part. It may be noted in passing that disastrous results may ensue if the treatment of uræmia comprise the withholding of water from the diet with the purpose of lessening the wateriness of the blood. Water is the best of diuretics and depuratives, and a remedy for uræmia, not a cause of it. It has been supposed, but probably erroneously, that increased intravascular tension is a necessary agent in bringing about the results of uræmia. It is not to be disputed that when this condition is advanced more or less over-tension is commonly present, but it is collateral rather than essential. With the uræmia of obstructive suppression, which, however it may differ from that of substantial renal disease, is truly toxic, tension is lessened rather than increased, and lardaceous disease occasionally ends in uræmia though the tension may have undergone no exaggeration.

It is sufficiently apparent that the condition of uræmia is not to be more narrowly defined than as one depending on the retention of urinary excreta; which excreta are especially injurious, or what changes any of them undergo to become so, are questions for the future.

I will now briefly indicate the symptoms and results of the uræmic state so far as it depends on the granular or fibrotic kidney, or, in other words, upon disease of long standing and not lardaceous.

Many of the results of renal disease—the vomiting, the inflammations, the asthma—must be held to depend on toxic retention, and be truly uræmic in their nature; certain conditions, not necessarily of nervous origin, may be first touched upon as indicating advanced uræmia, and apt to precede the cerebral manifestations. One of these is a brownish discoloration of the skin, especially of the face, which gives a sort of tropical look very different from the pallor of the less chronic varieties of renal disease. Itching of the skin is a late uræmic manifestation. It has been found in rare instances that crystals of urea have formed on the skin and hair in advanced cases of uræmia. This condition is associated with abnormal sweating, but the opposite condition sometimes presents itself, morbid dryness of the skin which refuses to perspire even under baths and other sudorifics. This is a late result and a bad indication. Another bad sign is advancing poverty of urine, which may be of low specific gravity, pale colour, often feebly acid or alkaline in reaction and of a fishy smell. The breath, under similar circumstances, assumes a characteristic, somewhat ammoniacal odour, and gives an ammoniacal reaction when brought in contact with hydrochloric acid.

A late uræmic manifestation of more than ordinary interest and more than ordinary distress is *uræmic asthma*. The patient, who probably has a hard pulse and a large heart, but whose breathing at ordinary times is normal or nearly so, is suddenly seized in the early part of the night, perhaps after having slept soundly, possibly without having slept at all, with agonising dyspnœa. The attack is like one of bronchial asthma with cardiac superadditions. There is agonising want of breath, with violent inspiratory effort and imperative orthopnœa. There is much palpitation and cardiac distress, apprehension, and a sense of mortal struggle. The patient perhaps clutches at the furniture, his face is bedewed with sweat and wears an expression of agony. Under such an attack I found in one case, together with much exaggeration of cardiac action, an intense blowing murmur, at the apex and systolic, which was not present before the fit and subsided soon after it. In another case I found during the attack a marked reduplication of the first sound which was not there before. After a term of agony and terror lasting, perhaps, two hours, the difficulty yields with wheezing, coarse crepitation, and the expectoration of frothy fluid, sometimes blood-tinged or accompanied with separate sputa of bloody mucus. With this the dyspnœa and distress subside, the respiration resumes its former tranquillity, and nothing remains of the paroxysm but the prostration which it leaves behind it. The foregoing sketch is drawn from cases of exceptional severity; many lesser degrees of the same condition are not infrequently met with. In the post-mortem examinations which I have seen after such attacks there has usually been emphysema, with injection and thickening of the bronchial membrane, and frothy or muco-purulent secretion in the tubes. In one instance the lungs were numerously beset with punctiform extravasations of blood. It is clear that these attacks are not ordinary asthma; they occur in persons who have not hitherto been asthmatic, and without any ostensible reason excepting the renal disease and its cardio-vascular complications. The bronchi may take some part in them, as is suggested by the bronchial secretion with which they terminate, but it cannot be doubted that the cardio-vascular system is essentially concerned, and uræmia the essential cause. I ventured, in the second edition of my book on *Albuminuria*, published in 1877, to suggest that spasm of the pulmonary artery was the *modus operandi* of the attacks under consideration; this hypothetical explanation has found favour with later observers, and may be regarded as probable, though not proved. The vascular contraction may be presumed to be in the smaller ramifications of the pulmonary vessel. It is known, but not always sufficiently regarded, that dyspnœa as intense as ensues from any obstacle to the admission of air to the lung may be produced by the cutting off of the blood from it. This is sometimes witnessed in cases of pulmonary embolism.

Proceeding to the specially nervous results of uræmia, one of the first to be observed is headache, which is often of a neuralgic type, intermitting, and sometimes of agonising severity. This often presents itself long before the fatal issue, and may constitute the chief ostensible symptom of the disease. Various other disturbances may occur towards the close of the malady, some peculiarity of or change in manner or temper, a lachrymose tendency, a feeling of stupidity, drowsiness, sometimes sleeplessness, and occasionally a horrible restlessness which is more distressing than any actual pain. Speech is now and then slightly affected in the way of indistinct articulation or clipping of words before the final overthrow of the nervous system, and sometimes, though rarely, there are at the same period symptoms, such as squinting or inequality of the pupils, which would seem to indicate, what may not be apparent after death, some localised change in the brain. As the scene approaches its close and the curtain is about to fall, other disturbances of intellect and nervous function may befall the actor. Such are many degrees of transient mental failure, to which such terms as "wandering" and "rambling" are applied. Occasionally there are hallucinations, brief delirium, or what must be regarded as transient insanity, delusions without fever. Among the consequences of advanced uræmia must be mentioned what has been termed Bright's blindness, partial or complete loss of sight, which may be temporary, which occurs independently of any retinal change or any alteration to be discerned with the ophthalmoscope, and cannot as yet be further defined than as a profound and ill-understood manifestation of the uræmic state. Various muscular agitations accrue and are often heralds of epileptiform convulsions, twitching of the face and limbs, subsultus, and tremor of the tongue. The end is now in sight, it occurs with coma sometimes, but not always, preceded by or accompanied with epileptiform convulsions. The "head symptoms" with the granular kidney do not differ materially from those which occur in nephritis, excepting that with the more chronic condition they are more uniformly fatal, and convulsion is relatively less frequent. Of 33 such cases convulsions were noted in 14, coma without convulsion in 19. The final uræmic attack sometimes comes on with little or no notice. It is not unknown for a man to fall in the street in what appears to be

DISEASES OF THE KIDNEYS

GENERAL PATHOLOGY OF THE RENAL FUNCTIONS

A. The Urine

In health the composition of the urine remains fairly constant, with some fluctuation in the amounts of the individual constituents. In disease the changes in its composition are due either to morbid processes in the kidney itself interfering with its excretory functions, or to changes in the general tissue metabolism producing substances not normally found in the economy; and these, after circulating in the blood, are excreted in the urine Not infrequently the excretion of these bodies in the urine may injure the kidneys. Disease may alter the quantities of normal constituents of the urine, or it may lead to the presence in it of abnormal substance.

Urinary water.—The quantity of water voided by a healthy adult in 24 hours is from 40 to 50 ounces. These limits may be exceeded or not reached; the quantity may rise to 80 or fall to 20 ounces In health, inasmuch as the water in the tissues remains fairly constant, the quantity of the urine is affected by (i.) the amount of fluid consumed, (ii.) the amount of fluid eliminated by other channels, as by the lungs, skin, and alimentary canal.

In disease the amount of water in the tissues may undergo great variations, and these variations will produce effects on the urinary flow; thus dropsy, from whatever cause, will necessarily lead to a diminution in the quantity of urine. Ultimately the amount of urine is determined in health by the functional activity of the glomerular tuft, and this in turn depends upon (*a*) the activity of the glomerular epithelium; (*b*) the rate of the flow of the blood through the tuft. Besides these two factors it is probable that the nervous system controls the kidney, so as to influence the amount of urine, and even to cause suppression.

The varying blood-flow through the kidney is, however, the factor about which most is known. Dilatation of the renal vessels, produced either through the nervous system, or on the direct stimulation of the blood-vessels by some chemical constituent of the blood circulating through the organ, causes a greatly increased flow of urine. The diuresis produced by local dilatation of the renal vessels is still further increased if the local renal dilatation is accompanied by a general constriction in other vascular areas. Conversely, local constriction of the renal vessels and general dilatation of all the other vessels of the body, by lessening the blood-flow through the kidney, cause a diminished flow of urine. Substances that produce an increased flow of urine—for instance, urea, sugar, caffein, and so forth—cause experimentally a dilatation of the renal vessels; but not always a simple dilatation: thus caffein produces an initial constriction followed by dilatation. Drugs like digitalis cause an increased flow of urine, although they produce constriction of the renal vessels; but here the result is due to the considerable rise in general blood-pressure and the increased velocity of the blood whereby, notwithstanding the constriction of the renal vessels, more blood probably flows through the kidney in a given time. The action of substances like urea, which cause diuresis with vascular dilatation, is a local one on the kidney, since all the effects can be produced after complete division of the renal nerves.

Although the state of the renal vessels is the factor in the secretion of urine with which we are best acquainted, my experiments show that the quantity of kidney substance has a profound effect on the amount of urine excreted. The removal of small portions either from one or both kidneys is followed by an increase in the quantity of urine secreted; and if so much as two-thirds of the total kidney weight be removed, the urinary flow may be permanently doubled without undergoing any other alteration in its composition. If a considerable wedge be removed from each kidney a still greater increase of the urinary water is obtained. The removal of three-fourths of the total kidney weight is followed, not only by a still greater increase in the urinary flow—so that it may be quadrupled in amount—but also by an augmentation of the excretion of urea. These observations show that the removal of portions of the kidney influence the amount of urinary water excreted very materially; and this notwithstanding the fact that the remnants of kidney do not undergo any marked pathological change.

Although no nerves have been found that exercise any influence on the secretion apart from the vaso-motor mechanism, yet no doubt the secretion of urine may sometimes be totally arrested without any great effect being produced on the renal circulation at the same time. To expose the ureter and put a canula into it will sometimes completely arrest the secretion of urine. On the other hand, puncture of the medulla causes a great increase in the amount of urine; and although the effects of the latter experiment may be explained as a result of vaso-motorial influence, this cannot be the case in the former, since there is no experimental evidence that interference with the ureter leads to any circulatory changes in the kidney.

In disease the quantity of the urine may be increased or diminished—the latter more usually than the former. If increased, the increase may be either permanent or temporary. In diabetes mellitus and in diabetes insipidus the increase is permanent. In lardaceous disease of the kidney and in renal cirrhosis the increase, although not present throughout the disease, yet persists for considerable periods. In chronic parenchymatous nephritis, or diffuse nephritis, considerable temporary increase is seen the blood is present in large quantities it will impart a bright red colour to the urine, notwithstanding its renal origin.

In very profuse hæmorrhage from the kidney and from the renal pelvis clots may form and temporarily block the ureter, and the patient may suffer from attacks of renal colic. Casts of the ureter may sometimes be passed.

The bladder is a common source of blood in the urine, and vesical hæmorrhage may be so profuse that the organ may become distended with blood-clots. In vesical hæmorrhage the blood may be uniformly mixed with the urine, but very frequently the blood is only seen, or is seen more abundantly in the last portions of urine passed, the first portions being quite clear. In prostatic hæmorrhage the bleeding is also apt to be seen at the end of micturition. Hæmatin is often found in the urine in cases of vesical bleeding, the blood having been decomposed by the acid urine.

A small amount of blood in the urine associated with a large amount of albumin points to the existence of renal disease. The blood in the urine may, by the eye, be confounded with bile and with urobilin. From the former it may be distinguished at once by the greenish tinge always seen on the surface of urine containing bile. From urobilinuria the mistake may be avoided at once by spectroscopic examination. Blood is most readily detected by microscopic examination of the lower strata of the urine after settling or centrifugalising. The blood corpuscles may be seen either but little altered or crenated; occasionally in dilute urine they may be distended and difficult to recognise as blood corpuscles. As confirmatory tests the guaiacum test, Heller's test, and the spectroscope may be used; but the last is not of much avail when traces of blood only are present. Hæmin crystals may also be formed, and afford a very certain indication of the presence of blood.

Hæmoglobinuria.—Here the colouring matter only of the blood, more or less altered, is found in the urine. It is exceptional for hæmoglobin to be present alone; it is usually mixed with methæmoglobin. The redder the urine, the greater the amount of hæmoglobin; the browner, the more methæmoglobin. It is possible that in many cases hæmatin is also present. Hæmoglobinuria is seen under the following conditions:—

(*a*) Paroxysmal hæmoglobinuria or *hæmoglobinuria a frigore.* In sufferers from this disease exposure to cold is followed by the disappearance from the circulation of very large numbers of blood corpuscles; thus, in an attack the patient may lose half the total number of blood corpuscles; the urine is as dark-coloured as porter, and contains no blood corpuscles, but a granular débris and oxalates. It is loaded with albumin, and the brown colour is due to a mixture of methæmoglobin, hæmoglobin, and urobilin. As the attack passes off the urine becomes of a lighter and redder tint, and finally returns to its normal colour.

(*b*) So-called symptomatic hæmoglobinuria. This is a condition where the hæmoglobinuria is simply an accompaniment of another malady. Thus it is occasionally seen in malaria and in Raynaud's disease, Suppression is not an uncommon sequel of catheterisation, when the kidneys are diseased secondarily to mischief in the lower urinary tract.

Obstructive suppression is seen in bilateral calculous disease, and where after one kidney has been practically destroyed by calculous pyelitis the ureter of the only active kidney becomes blocked by stone. It is also seen where, owing to disease in the pelvis, as in carcinoma of the uterus, both ureters are simultaneously closed. In these conditions the first effect is not suppression, but rather the production of hydronephrosis; no urine is emitted, but it is still secreted by the kidney. Sooner or later, however, if this condition be not relieved actual suppression ensues.

Specific gravity.—The specific gravity of the urine is usually from 1015 to 1025, but it may fall as low as 1002 persistently, as in diabetes insipidus, or it may rise as high as 1060. Persistently low specific gravity, especially in the urine voided in the early morning, or in the urine of the total twenty-four hours, is produced by such diseases as diabetes insipidus, cirrhosis of the kidney, lardaceous disease of the kidney, chronic diffuse nephritis, hydronephrosis, cystic kidneys. Severe Bright's disease, however, sometimes even fatal Bright's disease, can exist with a urine having a specific gravity as high as 1025.

The specific gravity is raised by the presence of large quantities of urea and salts in the urine, and by sugar. A character of the presence of the last substance, however, is a high specific gravity of a pale, dilute-looking urine; thus, a specific gravity of 1035 in pale urine suggests sugar, but a specific gravity of 1035 in a high-coloured febrile urine would have no such significance. Sugar may, however, be present, even in a considerable quantity, with a specific gravity as low as 1010; and when the specific gravity is raised by the presence of sugar the two do not necessarily vary together. A higher percentage of sugar may be present with a rather lower specific gravity. This is due to the effect on the specific gravity of other constituents, and more especially of urea and salts. In diabetes, provided the flow of urine be large and hence dilute, the specific gravity gives a fairly accurate notion of the quantity of sugar; but this is not the case if the quantity of urine be comparatively small.

Reaction.—The reaction of the normal urine is acid, but the acidity varies largely under the influence of meals. Although the urine voided in health is usually acid, the urine secreted by the kidney undergoes greater fluctuations in reaction. Thus, the morning urine is highly acid; the urine secreted two to three hours after a meal may be even alkaline, but probably, owing to admixture with acid urine in the bladder, the fluid voided will still be acid. The reaction of the normal urine is most influenced by diet; and, speaking broadly, an animal diet increases the acidity and a vegetable diet diminishes or even annuls this reaction. The acidity of the total urine in twenty-four hours in health is equivalent to two grammes of oxalic acid, and is dependent upon the presence of acid phosphate of soda. Probably as meat contains a considerable amount of this acid phosphate it is this constituent of meat which increases the acidity of the urine.

If in disease the quantity of urine be diminished, as in fever, the relative acidity is increased.

Patients living "high" and suffering from so-called lithæmia also excrete highly acid urine. The urine in diabetes, more especially in diabetic coma, the so-called acetonæmia, is highly acid, and is said to contain a number of abnormal acids, more especially β-oxybutyric acid.

In disease the acidity of the urine is more frequently diminished, and not uncommonly it is alkaline. The acidity is greatly diminished in cases of dilated stomach, and especially, it is said, as the result of washing out the stomach.

Two varieties of alkaline urine are recognised—one where the alkalinity is dependent upon the presence of a fixed alkali, and the other where it is dependent on the presence of a volatile alkali. The former is often associated with a diet rich in vegetable matter, and it is sometimes seen for long periods in nervous, dyspeptic, neurasthenic, hypochondriacal patients. Such urine is frequently milky from the precipitation of phosphates, more especially calcic phosphates. It is not a condition of any very great consequence, except that it may possibly lead to the precipitation of amorphous tricalcic and also of monocalcic phosphates, and may cause the formation of some of the rarer phosphatic stones.

Alkalinity from volatile alkali, on the other hand, is a very serious condition, and is usually dependent on decomposition of the urea into carbonate of ammonia, owing to microbic infection of the urine, usually from the introduction of dirty catheters. Sometimes the infection reaches the urine from within, owing to the rupture of an abscess into some part of the urinary tract; and it is perhaps possible that occasionally organisms may reach the urinary bladder, either by ascending the ureter or even by passing through the kidney from the blood. Alkaline urine loaded with bacteria is occasionally seen in Bright's disease.

Normal pigments.—Attempts have been made to explain the colour of the normal urine as dependent upon a single pigment, but at the present time there can be no doubt that several pigments are present, and, further, that the yellow colour is not dependent upon any substance yielding a banded spectrum. Normal fresh urines, when examined spectro-photometrically, show relative as well as absolute variations in the extension coefficient for any part of the spectrum. In this respect opinion has reverted somewhat to the earlier views of Schunk and Thudichum. The following pigments have been obtained from normal urine:—

Urobilin, a pigment obtained from the urine by precipitation with lead salts and subsequent extraction with alcohol acidified with sulphuric acid; or by saturation of the urine with ammonium sulphate. Urobilin is readily soluble in chloroform, and yields a definite absorption band at F. Some observers think that the yellow colour of the urine is dependent upon this body; others that, although it is undoubtedly present in normal urine, yet, as only traces are present, it plays an unimportant part in the production of the normal colour. The main facts in support of this latter view are that, whereas urobilin itself is freely soluble in chloroform, chloroform does not take up the yellow colour of normal urine; and that, whereas urobilin yields a very definite and dark absorption band at F, normal urine, even when viewed in deep layers, only shows a shading here. To account for the small amount present normally, and also for the fact that this amount is increased by exposure, oxidisation, and the like, it has been assumed that a mother substance, or chromogen of urobilin, is present in normal urine, which yields urobilin on oxidisation. Urobilin is present in the bile, and is probably identical with hydrobilirubin, formed from bilirubin by the action of potash and sodium amalgam. It is also identical with the body formed from acid hæmatin by the action of zinc and hydrochloric acid.

Uroerythrin.—This is the pigment that causes the pink colour of the uratic deposits, seen occasionally even in health. This pigment can be extracted from normal urine by means of amylic alcohol. It is an amorphous reddish substance, acid in reaction, soluble in alcohol, ether, and water. The alcoholic extract of pink urates yields two absorption bands between D and F. Uroerythrin, treated with caustic alkalies, yields a green colour.

Hæmatoporphyrin.—This pigment has been found by several observers in the urine as a result of the administration of sulphonal; and afterwards by Dr. A. Garrod as a trace in normal urine. Urohæmatoporphyrin was described by MacMunn as a pigment present in the urine in certain diseases; but it has been asserted that it is really a mixture of hæmatoporphyrin and urobilin—this body or bodies being present in traces only.

Urochrome.—None of the above-mentioned pigments, although present in normal urine, will account for the yellow colour of the fluid, and to a substance yielding a yellow solution, but not yielding any bands spectroscopically, Dr. Thudichum gave the name of urochrome. Recently this observation has been revived and extended by Garrod. Thudichum obtained a substance forming yellow crusts, freely soluble in water, fairly so in ether, less in alcohol. Schunk found two yellow pigments, one soluble in ether, the other not. Garrod has obtained an amorphous brown substance, insoluble in ether and chloroform, freely soluble in water. Although there are differences in solubility between the results of these various observers, there can be no doubt that they all operated on the same substance, and that this yellow pigment does not yield a banded spectrum; moreover, by Garrod's method at any rate, the urine was not acted upon by powerful reagents, capable of causing decomposition of the pigments present. Hence urochrome is probably the substance to which urine owes its colour.

Humous pigments.—Normal urines are found to darken materially when treated with mineral acids, and amongst the various pigments that are formed under these circumstances the so-called humous pigments described by Udranzky must perhaps be included. These are dark brown pigments, formed when carbohydrates are treated with acids or alkalies. They yield no bands, and they are soluble in amylic alcohol and in caustic alkalies; inasmuch as the normal urine contains carbohydrate derivatives it is quite possible for these substances to be formed.

The urine, in addition to the pigments described above, contains several other substances which, although not coloured themselves, yield well-marked and characteristic pigments on treatment with acids. The most important of these are the indoxyl and skatoxyl sulphates of potash.

Indican.—Indigo, as such, does not appear in normal urine, but in exceptional cases in decomposed urine it is seen in quantity sufficient to give the liquid a blue colour. It exists in the urine as indican, a compound of indoxyl, sulphuric acid and potash. Indoxyl is also said to be present in the urine in combination with glycuronic acid; as much as 20 mgrms. of indigo may be passed daily in the urine under normal conditions. The indigo owes its origin to indol formed in the intestines from proteid decomposition. Indigo is readily obtained from the urine by treating it with an equal volume of hydrochloric acid, and adding a solution of calcium hypochlorite, drop by drop, avoiding any excess. If the urine is then shaken with chloroform, the latter dissolves the indigo. Indigo is occasionally seen in urinary sediments and calculi. In disease the indican of the urine is greatly increased in cases where there is considerable intestinal putrefaction. Thus it is increased in constipation and in cases of long-continued intestinal obstruction. It is, however, seen also in cases of putrid inflammation; for example, in putrid empyema and gangrenous pneumonia, also in tuberculous peritonitis, gastric ulcer, cancer, and other diseases.

Skatol pigments.—These have a similar origin to the indol pigments; part of the skatol formed in the intestine yields potassic skatoxyl sulphate, and is excreted in the urine. On treating urine containing this body in abundance with an acid, the fluid becomes of a deep red colour. This pigment, like indigo, is present in increased amounts in the urine in constipation; and this perhaps accounts for its presence in diabetes and in chlorosis.

Abnormal pigments—In disease normal pigments may be excreted in greatly increased quantity; or again pigments, not normally present, may be excreted. Amongst the latter hæmoglobin and its derivatives, and bile pigments may be mentioned.

Urobilin.—As stated above, the normal urine contains only traces of urobilin; but in a great number of diseases urine is voided of a reddish brown colour and containing a large quantity of this pigment. To the eye the urine looks as if it contained bile or altered blood pigment; in fact this mistake is often made, more especially because such patients are often distinctly yellow, and the conjunctivæ are yellow. The stools, however, are of normal colour, and in testing the urine no bile reaction is obtained; on spectroscopic examination the deep black absorptive band at F, characteristic of urobilin, is seen. Some observers consider that this urobilin is different from the urobilin in normal urine, and that it only exists in the urine normally as a chromogen; to it the name of pathological or febrile urobilin has been given. There is considerable doubt, however, whether there is any distinction between the so-called normal and so-called pathological urobilin, and I have therefore used the name urobilinuria, as I believe that the substance is the same as the so-called normal urobilin, but that it is present in greatly increased amount. The important point is that in disease this pigment may be found in the urine in such quantity as to cause a superficial resemblance to bile-stained urine.

Urobilinuria is seen after copious internal hæmorrhage, such as follows the slipping of ligatures after abdominal operations, ruptured tubal gestation, or pelvic hæmatocele. In pernicious anæmia it is this pigment that causes the well-known brown colour of the urine, and also the lemon-tinted skin, conjunctivæ, and fat; and here probably it has the same origin, that is, the destruction of hæmoglobin. Urobilin is also found in the urine in increased amount in cirrhosis of the liver, with or without the presence of jaundice and of bile pigments in the urine. In febrile diseases the dark colour of the urine is due in part to excess of urobilin; and in paroxysmal hæmoglobinuria urobilin, in addition to hæmoglobin derivatives, has been found in the urine.

The hæmoglobin of the blood may be passed in the urine in the form of blood corpuscles, or it may be separately present. The former is usually spoken of as hæmaturia, the latter as hæmoglobinuria; although the latter is frequently a mixture of hæmoglobin with various derivatives, such as methæmoglobinuria, acid-hæmatin.

Hæmaturia.—Here blood corpuscles are present in the urine in varying amount. Blood may be added to the urine for purposes of deception; otherwise hæmaturia is due to hæmorrhage into some part of the urinary tract. Hæmorrhage from the kidney may come either from the kidney substance or from the renal pelvis. The former is seen in acute nephritis and in infarction of the kidney, passive congestion, or tumours; the latter in pyelitis, in calculous and tuberculous disease. Profuse hæmorrhage is sometimes seen in cases of purpura hæmorrhagica; probably it comes from the vessels in the loose cellular tissue of the renal pelvis, as in fatal cases copious submucous hæmorrhages are seen in this situation. In granular contracted kidney very profuse hæmorrhage is sometimes seen, so that the urine is bright red in colour; and here also it is probable that the hæmorrhage is really from the renal pelvis and not from the kidney itself. In cases where the hæmorrhage is actually from the kidney substance the urine will contain renal casts and very probably blood-casts. When the blood comes from the kidney or pelvis of the kidney, the blood is intimately mixed with the urine; and if it is present in small quantities only, the urine will be smoky from the action of the acid salts of the urine on the blood pigment, some of the hæmoglobin being converted into acid-hæmatin and methæmoglobin. If the blood is present in large quantities it will impart a bright red colour to the urine, notwithstanding its renal origin.

In very profuse hæmorrhage from the kidney and from the renal pelvis clots may form and temporarily block the ureter, and the patient may suffer from attacks of renal colic. Casts of the ureter may sometimes be passed.

The bladder is a common source of blood in the urine, and vesical hæmorrhage may be so profuse that the organ may become distended with blood-clots. In vesical hæmorrhage the blood may be uniformly mixed with the urine, but very frequently the blood is only seen, or is seen more abundantly in the last portions of urine passed, the first portions being quite clear. In prostatic hæmorrhage the bleeding is also apt to be seen at the end of micturition. Hæmatin is often found in the urine in cases of vesical bleeding, the blood having been decomposed by the acid urine.

A small amount of blood in the urine associated with a large amount of albumin points to the existence of renal disease. The blood in the urine may, by the eye, be confounded with bile and with urobilin. From the former it may be distinguished at once by the greenish tinge always seen on the surface of urine containing bile. From urobilinuria the mistake may be avoided at once by spectroscopic examination. Blood is most readily detected by microscopic examination of the lower strata of the urine after settling or centrifugalising. The blood corpuscles may be seen either but little altered or crenated; occasionally, in dilute urine they may be distended and difficult to recognise as blood corpuscles. As confirmatory tests the guaiacum test, Heller's test, and the spectroscope may be used, but the last is not of much avail when traces of blood only are present. Hæmin crystals may also be formed, and afford a very certain indication of the presence of blood.

Hæmoglobinuria.—Here the colouring matter only of the blood, more or less altered, is found in the urine. It is exceptional for hæmoglobin to be present alone, it is usually mixed with methæmoglobin. The redder the urine, the greater the amount of hæmoglobin, the browner, the more methæmoglobin. It is possible that in many cases hæmatin is also present. Hæmoglobinuria is seen under the following conditions:—

(*a*) Paroxysmal hæmoglobinuria or *hæmoglobinurie a frigore.* In sufferers from this disease exposure to cold is followed by the disappearance from the circulation of very large numbers of blood corpuscles; thus, in an attack the patient may lose half the total number of blood corpuscles, the urine is as dark-coloured as porter, and contains no blood corpuscles, but a granular débris and oxalates. It is loaded with albumin, and the brown colour is due to a mixture of methæmoglobin, hæmoglobin, and urobilin. As the attack passes off the urine becomes of a lighter and redder tint, and finally returns to its normal colour.

(*b*) So-called symptomatic hæmoglobinuria. This is a condition where the hæmoglobinuria is simply an accompaniment of another malady. Thus it is occasionally seen in malaria and in Raynaud's disease, and the phenomena are much the same as in the idiopathic hæmoglobinuria. It also occurs after severe burns and in acute infective diseases.

(*c*) Toxic hæmoglobinuria. This may be produced in poisoning by arseniuretted hydrogen, chlorate of potash, pyrogallic acid, naphthol, or carbolic acid.

Hæmoglobinuria is most easily recognised by spectroscopic examination; the bands of the methæmoglobin resemble those of oxyhæmoglobin, and, moreover, the band in the red is very characteristic of methæmoglobin. If the amount of hæmoglobin be large, and the urine be examined without dilution, only the band in the red will be seen, all the rest of the spectrum being cut off; but on dilution the two bands in the yellow will be seen, and care must be taken not to dilute too rapidly, otherwise the band in the red will be missed. Heller's test is also applicable. On microscopic examination of the urine, either no blood corpuscles or extremely few are seen. A number of droplets of a yellowish colour are frequently found. In fatal cases these are also seen in the cortical tubules of the kidney.

Hæmatoporphyrin.—This, as stated above, occurs in traces in normal urine, but occasionally in disease it is present in sufficient quantity to colour the urine a deep red or port wine colour. It has been observed in rheumatic fever, Addison's disease, peritonitis, and cirrhosis of the liver. It is also present in the urine after the administration of various drugs, more especially sulphonal. MacMunn considers that the pigment in the urine is not always hæmatoporphyrin or iron free hæmatin, but a modification of it, to which he has given the name of urohæmatoporphyrin. This pigment can be precipitated from the urine by barium chloride and barium hydrate, and extracted with acidified alcohol; the bands characteristic of it can then be seen on spectroscopic examination.

Melanin, a pigment containing sulphur, is rarely found in the urine. Occasionally urine of a *café au lait* colour is passed by patients suffering from melanotic sarcoma. On the addition of nitric acid to such urine it becomes black in colour, the chromogen of melanin being converted into melanin. Ferric chloride, when added to such urines, causes a grayish brown or black precipitate, soluble in excess of ferric chloride. Bromine water, when added to the urine, gives a yellow precipitate, which gradually blackens. Melanuria is occasionally seen in wasting diseases, apart from the presence of melanotic sarcoma.

Choluria.—In jaundice the bile pigments are found in varying quantity in the urine, and impart to it a colour varying from reddish brown to almost black. The upper surface of the urine, on an oblique illumination, has a greenish tinge, and on shaking such urine a greenish yellow froth is seen. Bile pigments can often be recognised in the urine in cases of jaundice before the yellow coloration of the skin is marked. The yellow colour of the skin may persist at a time when the pigmentation of the urine is slight or absent. It is held by some that bile pigments appear in the urine under the following conditions: (*a*) Obstruction of the bile-ducts, so-called hepatogenous jaundice; (*b*) Decomposition of hæmoglobin in the blood-vessels with the formation of biliary pigments, so-called hæmatogenous jaundice; (*c*) Decomposition of hæmoglobin after extravasation into the tissues and the formation there of biliary pigments. There is, however, some doubt as to the production of choluria under conditions (*b*) and (*c*). In many cases of decomposition of hæmoglobin either within or outside blood-vessels, large quantities of urobilin are excreted in the urine, and the urobilinuria so produced has a certain superficial resemblance to choluria. Some observers still assert that in hæmoglobinuria, and after large internal hæmorrhages, bile pigments appear in the urine along with the urobilin and methæmoglobin. However this may be, the great bulk of cases of choluria undoubtedly depend upon obstruction of the bile-ducts, large or small. Although bile pigments are present in the urine in obstructive jaundice, and are readily recognised, this does not apply to bile salts; and even in cases of complete and permanent obstruction of the bile-ducts it is difficult to detect them in the urine unless special methods are employed. For the recognition of bile pigments Gmelin's nitric acid test is the best; but the acid should not contain too much yellow fuming acid, as with this the oxidation occurs too rapidly, and the play of colours is not readily seen. The test can be performed on a plate or blotting-paper or on a slab of plaster of Paris. These methods are all better than pouring the urine on the nitric acid in the bottom of a test-tube. Bile cannot be said to be present unless a green colour is seen as the first colour in the play. Bile pigments may be precipitated with milk of lime, the precipitate collected and treated with water, and then shaken with chloroform acidified with acetic acid. The chloroform solution of the bile pigments may then be used for Gmelin's reaction. The recognition of the bile salts in the urine is more a matter of scientific than of clinical interest [*vide* "Functions and Functional Disease of the Liver"]. Occasionally their presence may be recognised by Pettenkofer's reaction in the urine itself, that is, by treating the urine with a solution of sugar and some sulphuric acid, and shaking; the purple colour characteristic of the reaction may be seen in the froth. More usually this procedure fails, and then some ounces of urine must be evaporated to dryness, the residue extracted with alcohol, the salts precipitated by ether, dissolved in water, and Pettenkofer's reaction sought with this solution. To the eye, urine containing bile may be confounded with urine containing large quantities of urobilin, and with urine containing decomposition products of hæmoglobin, such as methæmoglobin and hæmatin.

It is of interest to note that in cases of external biliary fistula, with complete obstruction of the bile-ducts, the urine maintains its normal yellow colour, notwithstanding that all the bile secreted is passed outwards, and none enters the intestine. This fact throws considerable doubt on the view that the urinary pigments (urochrome, urobilin, etc.) are derived ultimately from the bile pigments.

Pyrocatechin and hydrochinon.—The former substance occurs normally in small amounts in the urine, and is greatly increased in cases of carboluria. The latter occurs only in cases of poisoning with carbolic acid. Both these substances exist in the urine as ethereal compounds of sulphuric acid. Urine containing pyrocatechin is colourless when passed, but darkens on exposure to the air; if this substance be abundant, the urine will become black. It is to this body and to hydrochinon that the greenish black colour of the urine in carboluria is due.

Nitrogenous extractives.—About 15 grammes of nitrogen are excreted daily on an average during health, and the most important nitrogenous constituents of the urine are urea, uric acid and *kreatinin*; others, such as xanthin, guanin, hippuric acid, although present, are not of great clinical importance.

Urea.—Normal human urine contains, roughly speaking, 2 per cent of urea, occasionally rising in health to as much as 3 per cent. The daily quantity excreted has been stated to vary between 22 and 40 grammes, the average being usually stated at some 30 grammes. Approximately 0·5 grm. of urea is excreted per kilogramme of body weight. Children excrete rather more relatively to their body weight. Normally the amount of urea excreted is largely dependent on the diet, and hence is greatly increased after meals. Copious water-drinking increases the urea excretion, at any rate temporarily. Exercise does not lead to any notable increase. In disease the excretion may be diminished or increased, and if increased, the increase may be absolute or relative, temporary or permanent.

Observations on the urea excretion in disease are of little value unless the amount and nature of the foods consumed be taken into consideration In diabetes mellitus the quantity of urea excreted is greatly and permanently increased, and here the increase is dependent largely upon the increased appetite and nitrogenous diet, partly also upon the wasting.

In diabetes insipidus the quantity of urea is also slightly increased. In febrile diseases the percentage of urea is greatly increased, owing to the density of the urine; and the amount is always relatively increased, since even if quantities of urea, equal to the normal, are excreted, owing to the failure of appetite the amount is really greater than that excreted by a patient with a normal temperature on the same diet.

In wasting diseases, such as cancer of the œsophagus and stomach, associated with vomiting and with practical starvation, the amount of urea is diminished; and this is the case also in diseases destroying the liver substances, as in atrophic cirrhosis; it reaches its minimum in acute yellow atrophy, where the urea may entirely disappear from the urine. In renal diseases the urea is diminished in cases of consecutive nephritis, where urine of a very low specific gravity is passed, which contains a very small percentage of urea. In acute nephritis also very little urea is passed, owing largely to the great diminution in the quantity of urine.

In chronic nephritis the amount of the urea excretion varies. In cases associated with dropsy, and where, therefore, but little urine is secreted, the quantity of urea excreted is small in amount; but in cases of chronic nephritis not accompanied with dropsy, and where there is no uræmia, the quantities excreted are often equal to those seen in health;

and in my experience I have found it is not uncommon for daily quantities of 30 grammes to be passed. It is usually held that in chronic nephritis a sudden and great diminution in the urine and urea excretion points to the imminence of uræmia.

In renal cirrhosis considerable quantities of urea may be passed, and it is not uncommon, in cases of this disease, for uræmia to occur at a time when the patient is passing large quantities of urea, quantities quite commensurate with the amount of nitrogenous food taken, although perhaps the amount is less than that passed by a healthy adult on full diet, such patients being usually on a low diet.

The quantity of urea is usually estimated for clinical purposes by the hypobromite method. This method, even when most carefully performed, gives erroneous results to the extent of 8 per cent. In performing a determination it is important that the hypobromite of sodium should be freshly prepared, that it should not be used in large excess, and that the mixing of the urine and the hypobromite should be carried out very slowly.

Other methods of estimation are those known as Liebig's and the precipitation with phosphotungstic acid. These methods, however, are not commonly employed in clinical work.

Uric acid.—This substance is excreted to the amount of 1 gramme a day. It is present in the urine in the form of a quadriurate. Uric acid is probably formed in the liver and spleen It is known definitely that it is formed in the liver of birds, but in the mammal the seat of its formation is largely a matter of inference, and it has been asserted that it is formed in the kidney. The amount excreted is largely increased by meals, and the increased excretion after meals is said to occur sooner than the increased excretion of urea. The increase after meals is not entirely dependent upon the nature of the meal, although a proteid meal is the one most likely to produce it. This increased excretion is most marked during the alkaline tide. All kinds of nitrogenous food lead to an increased excretion of uric acid; but it is not clear that large quantities of meat produce a greater excretion than vegetable food, although, owing to the acidity of the urine with a meat diet, and the relative alkalinity of the urine with a vegetable diet, the uric acid is perhaps more liable to precipitation.

All urines, if kept from putrefaction, deposit uric acid sooner or later; but if it occurs some twelve hours after the passage of the urine, its deposition has no clinical significance; if it takes place within this time, and more especially if it occurs within four or six hours or sooner, then it becomes important, inasmuch as it might occur whilst the urine is in the urinary passages, and so lead to the formation of a renal or of a vesical stone.

Uric acid is very insoluble in cold water (1 in 15,000), but more soluble in boiling water. Uric acid, in fact, derives most of its clinical importance from its insolubility. In a weak alkaline solution, such as 0·2 per cent of bicarbonate of soda, it is more soluble, owing to the formation of a quadriurate; but if this solution be allowed to stand, crystals of biurate of soda are deposited owing to the decomposition of the quadriurate.

Uric acid itself crystallises in the form of rhombic prisms, but the size and shape of the crystals vary with the relative purity of the liquid from which the crystals are formed; and the process is greatly modified by the presence of albuminous substances in the solution.

If precipitated by an acid from a solution in bicarbonate of soda, uric acid crystallises in plates; from the urine, however, the usual form is lozenge-shaped crystals. The crystals are usually brownish red in colour, from the taking up by the uric acid of some of the urinary colouring matter, more especially uroerythrin; and owing to this peculiarity, uric acid deposits are usually recognised at once by the naked eye.

The ultimate source of the uric acid of the urine is rather doubtful. Formerly it was held to be derived in part from the food, and in part from the proteid metabolism of the body. Now it is considered to be the end product of the metabolism of nuclein; hence it is possible that the destructive metabolism of the blood corpuscles, both red and white, may, in part at any rate, provide the uric acid daily excreted. On this view, the increased excretion after meals would be dependent upon the rapid destruction of the leucocytes associated with the mechanism of absorption. It must be remembered, however, that nuclein exists in the food as well as in the body.

In disease the uric acid excretion is diminished during the paroxysm of gout, but after the attack the amount excreted is increased. It is also said to be diminished in chlorosis and in most chronic diseases On the other hand, it is increased in pernicious anæmia, in splenic leukæmia, in febrile diseases, in ague, and in certain forms of diabetes mellitus, sometimes called gouty diabetes. In pernicious anæmia and in leukæmia the increase may be very great; thus, in the former, from two to three times the normal amount may be excreted when the patient is taking very little food; and in leukæmia the increase may be still greater The quantity excreted, however, is not so important as the rate of its deposition, since urines containing less than the normal amount of uric acid (for example, the urine of renal cirrhosis) may still deposit uric acid, so that the nature of the urine, its acidity, and the amounts of its salts and pigments are frequently matters of more practical moment than the amount of uric acid present.

The deposition of uric acid, as such, from the urine is influenced mainly by the acidity of the urine, the quantity of salts present, and the amount of pigment. The salts of the urine keep the uric acid in the form of a soluble quadriurate, hence dilute urines deficient in salts and colouring matter frequently deposit uric acid, whereas a concentrated highly acid febrile urine, containing a considerably higher percentage of uric acid, will lead to the formation of a deposit of urates.

The most delicate test for uric acid is the well-known murexide test. Uric acid or urates are treated with fuming nitric acid and, when cold, ammonia added; a beautiful purple-red colour is thus produced. Potash produced a purplish blue instead of a purple-red colour.

Quantitative estimation of uric acid.—In certain diseases, gout, pernicious anæmia, leukæmia, etc., it may be advisable to determine the quantity of uric acid present; for this purpose one of the following methods is usually employed:—

Heintz's method.—To 200 c.c. of filtered urine 10 c.c. of hydrochloric acid are added, and the mixture set aside in a cool place for forty-eight hours. The crystals are collected on a weighed filter, washed repeatedly, and dried at 100° C. This method is only approximately accurate, since some of the uric acid is retained in the acid and in the washings. Further, uric acid may be present in urine and yet not be precipitated by the addition of hydrochloric acid (Salkowski and Leube).

Folker's method.—This method is more accurate than the former, but also more tedious. 200 c.c. of urine are rendered alkaline by the addition of an excess of sodium carbonate. To this alkaline urine 20 c.c. of a strong solution of ammonium chloride are added. The mixture is allowed to stand for forty-eight hours and then filtered through a weighed filter. The urates are thus collected on the filter, and to them is added 10 per cent hydrochloric acid, the filtrate being returned again and again to the filter. Finally, the filtrate is allowed to stand and deposit crystals of pure uric acid in colourless plates, which are collected on the same filter, washed with water, then with alcohol, dried and weighed, and 03 grm added to the weight obtained.

Hopkins' method.—This method will probably replace all others; it is based on the fact that ammonium urate is insoluble in ammonium chloride. To 100 c.c. of the urine about 50 grms of powdered ammonium chloride are added, care being taken that some of the salt remains undissolved. After standing for two hours the precipitate is collected on a filter and washed with a saturated solution of ammonium chloride. The precipitate is washed into a small beaker with hot distilled water, and heated to boiling with an excess of hydrochloric acid. After standing for two hours the uric acid separates and is collected and washed on a filter and dissolved in a weak solution of sodium carbonate. The bulk of the liquid is now made up to 100 c.c., mixed with 20 c.c. of sulphuric acid, and titrated with one-twentieth normal potassium permanganate; 1 c.c. of this solution is equal to ·00375 grm. of uric acid.

Urates.—As mentioned above, uric acid is normally excreted in the form of a quadriurate, the bases being sodium, potassium, calcium, and magnesium. In health the quadriurates remain soluble, even when the urine cools; but if the quantity of urine be diminished, as the result of sweating, for example, then the urates are only soluble in the warm fluid, and in the cool become deposited in the well-known brownish red amorphous form. This in time is decomposed, and, provided the urine is not allowed to decompose, deposits crystalline uric acid. The decomposition of the quadriurate into biurate and uric acid is readily effected by distilled water; so that in order to collect the quadriurate deposit it must be washed and filtered with alcohol and not with water. Urates are abundant in febrile urines, and more especially towards the end of a febrile illness. They are also increased in dyspepsia and other diseases of the stomach, and in atrophic hepatic cirrhosis. Urates are also abundant in the dense high-coloured urines secreted in cases of venous congestion; as, for instance, in diseases of the heart and lungs. Occasionally the urates are present in the urine in a crystalline form, more especially the acid sodium and ammonium urate; the latter especially is apt to form crystals with spiny processes which, in the case of children, may cause considerable irritation in the urinary tract, and even in the urethra; and this may lead to the temporary suppression of urine.

In all dense high-coloured urine the risk of mistaking the reduction of copper produced by urates for the effects of sugar must be kept in mind As a rule, urates require longer boiling to reduce the copper, and they tend to produce a yellowish green deposit rather than the brick-red deposit seen with sugar. Reliance should be placed in doubtful cases on the presence of some other sugar test, such as the fermentation test and the phenyl-hydrazin test. Other nitrogenous constituents of the urine, such as xanthin, hypoxanthin, are not of sufficient clinical importance to be considered here.

Kreatinin, after urea, is the most abundant nitrogenous constituent of the urine; but, as its solubility is so great, it is a body of little interest to the clinician; thus, although there is twice as much kreatinin excreted as there is uric acid, yet the latter is of far greater importance.

The kreatinin of the urine is probably largely derived from the kreatin of the food, but it has also a tissue origin, for in wasting diseases it is considerably increased in amount. The main importance of kreatinin lies in the fact that it reduces copper like sugar, and hence, occasionally, its presence in the urine in unusual quantity may be mistaken for traces of sugar. Kreatinin and urates between them account for a large part of the reducing action of normal urine. The mistake of confounding kreatinin and sugar may be avoided, either by precipitating the kreatinin by mercuric chloride, or by testing for sugar by the fermentation test.

Leucin and Tyrosin.—These bodies, formed normally in the alimentary canal, are occasional constituents of the urine; more especially is this the case in acute yellow atrophy of the liver (p. 111), and in cases of phosphorus poisoning (vol. ii. p. 923). It was formerly thought that these substances were not present in the urine in phosphorus poisoning, so that by their means a differential diagnosis between phosphorus poisoning and acute yellow atrophy could be arrived at. Leucin and tyrosin have, however, been found in small amount in several cases of undoubted phosphorus poisoning (p. 90). Leucin and tyrosin have also been found in the urine, in small quantities, in cases of hepatic cirrhosis. It is to be remembered that in this disease widespread degenerative changes occur in the liver-cells, giving rise to a condition sometimes spoken of as secondary yellow atrophy; hence the presence of leucin and tyrosin in the urine is of interest in the pathology both of this malady and of acute yellow atrophy. When these bodies are present the amount of urea is generally much below the normal, and in acute yellow atrophy it may even be absent.

Tyrosin occurs both as crystals and also dissolved in the urine; the crystals are usually of a greenish colour, and are deposited in the form of sheaves and rosettes. Leucin, on the other hand, is usually found in crystalline globular masses. Crystals of calcic phosphate, of sodic phosphate, and of the lime and magnesium salts of fatty acids, are sometimes found in the urine in the form of sheaves and rosettes, and may be mistaken for tyrosin; but, in the case of the phosphates, the individual needle-like crystals are broader, and they are usually colourless. Reliance, however, should not be placed on the crystalline appearance alone, but some tests characteristic of tyrosin should also be employed.

Tests for tyrosin.—The best known of these are Piria's and Hoffman's reactions. Tyrosin when heated with Millon's reagent yields a brilliant crimson colour (Hoffman's reaction).

Tyrosin, if treated with concentrated sulphuric acid and warmed, gently turns pink. The mixture is allowed to stand, diluted with water, saturated with barium or calcium carbonate, and filtered while hot. On the addition of dilute perchloride of iron free from acid, the filtrate yields a violet colour (Piria's reaction).

Leucin is not readily recognised by chemical tests unless a considerable quantity of the pure substance is available, hence in the urine its presence is to be detected by its microscopic characters.

In cases in which leucin and tyrosin are found in the urine, lactic acid may also be present. This is true of the urine of phosphorus poisoning, and also in cases of acute yellow atrophy of the liver. The excretion of lactic acid in the urine, associated with the diminished excretion of the normal nitrogenous extractives in these conditions, resembles the condition brought about experimentally by the removal of the liver in birds; since after this operation the nitrogenous extractives in the urine fall to a very small amount, and lactic acid and ammonia are excreted.

Salts.—*Sulphates.*—Two grammes of sulphuric acid a day are excreted in normal urine, and the bulk of it is excreted in combination with inorganic bases, such as sodium, potassium, magnesium. Some of it, however, is excreted in the form of a double salt, one of these bases being usually potash in combination with certain aromatic bodies, such as phenol, cresol, indol, or skatol; these form the well-known aromatic sulphates or potash salts of phenyl-sulphuric acid.

A small quantity of sulphur is also excreted in combination with amides, forming bodies of the taurin (amido-ethyl-sulphonic acid) class. Cystin (amido-sulpholactic acid) is another example of these bodies. The amount of sulphur so eliminated is very small. The sulphates excreted as inorganic and as aromatic sulphates are derived in part from the food and in part from the metabolism of the tissue proteids; and their main clinical interest lies in the relation between the amounts of the aromatic and the total sulphates. Normally, the proportion existing between the aromatic and simple sulphates is approximately one part of the former to twelve to twenty parts of the ordinary sulphates. The aromatic sulphates are derived mainly from the decomposition of proteid matter, and largely from decomposition and putrefaction in the intestine. Hence the amount of aromatic sulphates excreted is considerably increased in intestinal and abdominal diseases associated with retention and putrefaction of the intestinal contents; as, for example, in intestinal obstruction, and in tuberculous and other forms of peritonitis. In typhoid fever they are said not to be increased. They are increased in cases where putrid decomposition of proteid matter arises, as in putrid empyema, pulmonary gangrene, and the like. In fact they are necessarily increased in cases of the kind which lead to indicanuria, inasmuch as indigo is present in the urine as an indoxyl sulphate. Aromatic sulphates are also greatly increased in amount in cases of poisoning by carbolic acid.

Cystin and cystinuria.—This sulphur-containing body is occasionally present in the urine, and it may even give rise to the formation of calculi. It crystallises in flat hexagonal plate-like tables, insoluble in acetic acid, but freely soluble in ammonia, and so differing from uric acid. Cystin burns with a bluish-green flame on platinum foil. If the crystals are boiled with caustic potash and oxide of lead, sulphite of lead is formed. Similarly, if heated with caustic potash on a silver dish or silver coil, a black mark is left on the silver from the formation of sulphite of silver.

The main interest of cystinuria lies in the fact that this condition is simply an excessive secretion of a substance closely allied to bodies which exist in traces in normal urine.

Phosphates.—Two to six grammes of phosphoric acid are excreted daily in the form of mixed phosphates of potash, soda, lime, and magnesium; and the acidity of the urine is dependent mainly upon the presence of acid sodium phosphate. A large quantity (two-thirds to three-quarters) of the phosphoric acid excreted is united with potash and soda, and, whether the salts formed be acid, neutral, or basic, they are soluble in the urine, and hence are not seen as urinary deposits.

Earthy phosphates of lime and magnesium are only soluble in acid urine, hence the neutral and basic phosphates of lime and magnesium tend to be deposited in faintly acid, neutral, and alkaline urines. In urines alkaline with ammonia ammonio-magnesic phosphate is formed, which is also insoluble. Ammonio-magnesic phosphate has been found deposited from urines still faintly acid. The phosphates are derived largely from the food, partly from the tissues. The amount of phosphates in the urine is largely increased after meals, and then, owing to the diminished acidity or even positive alkalinity of the urine, it is not uncommon for some precipitation to occur; the amount of deposit, however, is no index to the amount of phosphatic material present in the urine, inasmuch as its deposition depends simply on the reaction. In all cases, if the amount excreted is to be determined, reliance must be placed on quantitative methods of estimation, and not on the amount of deposit. To the clinician the main interest lies rather in the deposit of earthy and of triple phosphates than in the total amount of phosphates excreted; for the latter depend very largely on the quantity and nature of the food.

In febrile disease the quantity of phosphates excreted is at first diminished; later it is increased. It is held that in certain states of neurasthenia the quantity is increased; and the name of phosphatic diabetes has been given to a condition in which, along with general malaise and various neurasthenic symptoms, large quantities of urine, containing an excess of phosphates, are excreted [*vide* vol. iii. p. 253].

On heating urine faintly acid, neutral, or alkaline, a cloudy deposit of earthy phosphates is produced; or, if the liquid previously contained a deposit of phosphates, this is increased. If the liquid is not actually raised to the boiling-point, the deposit will redissolve on cooling; but if it be boiled, the deposit is permanent. If the boiling be done in a sealed tube, the precipitate can be produced and dissolved several times in succession. There are several possible explanations of this fact (*a*) That the boiling drives off the carbonic acid by which the phosphates were kept in solution; (*b*) That the boiling causes a decomposition to ensue of such a character that two molecules of dicalcic phosphate and one of monocalcic phosphate undergo an interaction, which leads to the formation of one molecule of triple and one molecule of dicalcic phosphate, the former of which, being far less soluble, is precipitated. (*c*) It has also been suggested that on boiling, sufficient urea is decomposed into ammonium carbonate to render the urine sufficiently alkaline to cause the precipitation of phosphates. It is improbable that the precipitation is simply dependent on the lower solubility of certain phosphatic salts in hot urine than in cold; and it is more likely that a decomposition of the nature described above ensues. The deposition of phosphates in the urine depends partly upon the amount present, but largely upon the degree of acidity of the urine. The deposition of earthy phosphates —for example, the tricalcic—is associated with an alkaline action due to fixed alkali. This deposit is amorphous, and is often seen after meals. Occasionally stellar phosphate—that is, dicalcic phosphate—is thrown down when the acidity of the urine is diminished; but it usually occurs in urine still faintly acid, it is rarely seen in neutral or alkaline urines. The crystals are frequently arranged in stars and rosettes, or in sheaf-like bundles, thus offering a distant resemblance to tyrosin crystals. This deposit is rarely seen in healthy urine; it occurs, however, in the urine of diabetes and of other maladies, such as cancer, which produce grave disturbance of nutrition. In urines alkaline from volatile alkali, a deposit of triple phosphate (ammonio-magnesic phosphate) is common; and this crystalline deposit frequently leads to the formation of a calculus enclosing most usually a nucleus of uric acid or of oxalate of lime that has been formed in the kidney and passed on to the bladder. This triple phosphate is also prone to encrust the surface of vesical growths; and it tends to be deposited whenever there is cystitis: the amorphous deposit of tricalcic phosphate, on the other hand, owing to its amorphous character, rarely forms calculi.

Chlorides.—Although these salts play an important part in the economy, and are excreted in the urine in abundance—10 to 15 grammes being the amount of the daily excretion of sodium chloride—the variations in the amount of chlorides excreted are not of any great clinical importance. They depend largely upon the amount of chlorides in the food. The principal fact is that the chlorides are diminished during the height of the pyrexia of febrile diseases; and more especially in pneumonia, where, during the duration of the fever, they may almost disappear from the urine to reappear again at defervescence and during recovery. The amount present does not afford any valuable indication as regards diagnosis or prognosis of febrile states, although it is in pneumonia especially that the chlorides undergo this great diminution. The same phenomenon is seen to a less extent in other febrile diseases, and more especially when the fever is high, as in tonsillitis, for instance, so that the diminished excretion is dependent rather on the general febrile process than on the particular incidence of it on the lung. To determine roughly the amount of chlorides present in the urine it is sufficient to acidulate the urine with nitric acid, to add a few drops of nitrate of silver, and to compare the precipitate obtained with the amount obtained by a similar procedure with normal urine. If necessary, the precipitate of chloride of silver may be collected and weighed in the usual manner employed in quantitative determinations.

Oxalates.—About 20 milligrammes of oxalic acid are excreted daily from the normal urine in the form of a salt kept in solution by the acid phosphate of soda normally present. Oxalates are deposited in the urine in the form of oxalate of lime, which tends to crystallise either in octohedra, or as dumb-bells or ovoids. The crystals are visible to the naked eye as brilliant points, and usually crystallise like uric acid on any irregularities, such as scratches on the glass vessels in which the urine is contained. Urine depositing oxalate of lime is usually acid, rarely neutral. The dumb-bell form of crystals deposited is perhaps due to the disturbance of the form of crystallisation by mucin and other colloids present. A scanty deposit is not unusual in health, and more especially after certain articles of diet, such as rhubarb and other vegetables. A persistent deposit, however, is pathological, although it is not clear upon what this oxaluria depends. The name oxaluria ought, of course, to be restricted to an increase of the excretion of oxalic acid, and not simply to its deposition. In many cases the increased excretion or deposition of oxalic acid may lead to the formation of an oxalate of lime calculus, without the production of any other symptoms except those due to the stone. In other cases the persistent excretion of these insoluble oxalates is accompanied by a series of symptoms of a dyspeptic character, together with some mental depression, neurasthenia, or even actual hypochondriasis, and it is not clear whether there is any definite cause of association between the two sets of phenomena, although many observers regard the dyspeptic, nervous, neurasthenic symptoms as primarily due to the oxaluria.

Albuminuria.—The name albuminuria is generally taken to signify the presence of proteid matter in the urine. The proteids met with in the urine are serum albumin, serum globulin, albumose, peptone, fibrin, nucleo-albumin, and perhaps occasionally a casein like body, and, if blood or blood pigment be present, hæmoglobin. In health the urine is free from any large quantity of proteid matter, although in some 30 per cent of persons apparently healthy the urine is found to contain proteid matter in small quantities. To this condition the name of *physiological albuminuria* has been applied. This albuminuria is, in some of the cases, always present; in others, it appears only under certain conditions, as, for instance, on first rising in the morning, after a cold bath, or after meals. Some of these varieties have received special names; such as intermittent albuminuria, dietetic albuminuria, postural and cyclic albuminuria.

Albuminuria is either "physiological" or pathological; by the former it is understood that in apparently healthy persons albumin—usually in small quantity—is found in the urine; sometimes so little that it requires special tests, such as picric acid, to reveal it; at other times it is in sufficient quantity to yield a distinct precipitate with the heat test or with cold nitric acid. In these cases it is important to exclude what may be called accidental albuminuria, cases, that is, in which the urine itself, originally free from albumin, has been contaminated by some albuminous impurity, as in gonorrhœa, vaginitis, and seminal discharge.

Probably in no case of so-called physiological albuminuria is the quantity so large as to amount to one-third or even one-fourth of the urine. This albuminuria in the apparently healthy is not necessarily continuous. It may be seen only after meals, and more especially after breakfast, or on first rising in the morning, or after severe exercise. It is supposed in many cases to depend upon a vascular disturbance in the kidney, leading to temporary venous congestion; and in the dietetic cases it has been thought that digestive products, such as albumoses, might be formed, either in greater abundance than usual, or else of abnormal quality, and, absorbed as such, be subsequently excreted by the kidney. It is extremely doubtful, however, whether such cases of albuminuria should be called "physiological." It is quite possible that, in many such cases, no serious kidney lesion is present, nor yet, perhaps, any condition likely to eventuate in a serious kidney lesion; yet, on the other hand, such kidneys cannot be considered quite sound. In a considerable proportion of cases of "physiological albuminuria" the use of the centrifuge shows that the urine contains definite formed elements, such as white blood corpuscles, casts, spermatozoa and so forth. In other words, the presence of casts in small amount is not restricted to "pathological albuminuria." It must be remembered that in renal cirrhosis the urine may contain only traces of albumin; and the possibility of the presence of this insidious disease in some cases of so-called functional albuminuria must be kept in view.

Pathological albuminuria.—Albuminuria may be due to disease of any part of the urinary tract, such as pyelitis or vesical disease; but in these cases, to speak strictly, the albuminuria is factitious and is due to admixture with albumin after the urine has left the kidney. When the albuminuria is of renal origin, the albumin transudes into the urine, owing to some definite lesion, temporary or permanent, of the kidney epithelium. Sometimes the kidney lesion is primary, at other times it is secondarily induced by the ingestion or production of toxic and irritating substances in other parts of the body. At other times, again, the changes in the kidney are dependent upon other secondary disturbances, thus the following causes of albuminuria may be recognised:—

(*a*) Congestion of the renal vessels, active or passive.

(*b*) Toxic or febrile albuminuria.

(*c*) The albuminuria of organic renal disease, such as acute nephritis, chronic Bright's disease.

(*a*) Active congestion.—The loss of albumin in this condition is usually not large, as the quantity of urine secreted is small and often blood-stained. It is difficult to distinguish the albuminuria of active congestion from that due to toxic agents, as in many cases poisons, such as turpentine and cantharides, produce extreme congestion. The albuminuria of acute Bright's disease is usually quoted as an instance of this form of albuminuria.

Passive congestion is a frequent cause of albuminuria, more especially in heart and lung diseases, and as the result of various abdominal diseases leading to pressure on the renal veins or vena cava. Passive congestion causes a considerable diminution in the quantity of urine secreted, and this may contain blood and blood-casts. In cases of pressure on the renal veins from abdominal diseases the percentage amount of albumin present may be large, but in cardiac and pulmonary cases the quantity is usually small. From the mere amount of albumin, however, no conclusion can be drawn as to whether the albuminuria be due to passive congestion or to nephritis. It may be large in the former and small in the latter, or conversely. Blood may be present in either case. The question is best answered by the character of the casts present. In passive congestion blood-casts and hyaline-casts are occasionally found; in nephritis, on the other hand, casts containing definite renal elements are found.

(*b*) Febrile or toxic albuminuria.—This is dependent, in all probability, on the excretion by the kidney of toxins produced by the organisms causing the disease. These toxins apparently lead to changes in the renal epithelium, glomerular and tubal, and thus allow the proteids of the blood-plasm to pass out. In this way the febrile albuminuria resembles the albuminuria produced experimentally by the injection of egg-albumin, albumoses, or peptones. The proteid matter found in the urine subsequent to this procedure is not only the albumose or other proteid injected, but also the proteid matter of the blood-plasm; and the amount of proteid recoverable from the urine is frequently far greater in amount than the quantity injected. Thus the albuminuria brought about by the intravenous injection of these proteid substances resembles the albuminuria due to such poisons as cantharides. On the other hand, many toxins produced in disease apparently do not cause the extreme congestion that is seen with such poisons as cantharides. In scarlet fever, the early albuminuria of the disease, which is of this nature, must be carefully distinguished from the later albuminuria dependent upon nephritis often persistent and progressive. The kidney lesion that produces the albuminuria of febrile diseases, often spoken of by French writers as transitory nephritis, is remarkable, inasmuch as this lesion generally disappears completely, leaving the kidneys practically healthy. In this respect the initial albuminuria, or so-called febrile albuminuria, of scarlet fever is strikingly different from the later albuminuria, which is dependent on a progressive and destructive lesion in the kidney. In the great majority of cases the changes produced in the kidney by these toxins do not lead to permanent Bright's disease; and the albuminuria of typhoid, scarlet fever, diphtheria, and pneumonia usually clears up entirely. Occasionally in typhoid fever, diphtheria, and pneumonia, and very frequently in scarlet fever, there is a further and more severe lesion produced in the kidney, and the case becomes one of acute or subacute nephritis, with dropsy and suppression of urine. Hence it is difficult to draw a hard and fast line between the febrile albuminuria produced by toxins, or the *nephrite passagère* of the French, and a permanent and often progressive lesion like Bright's disease.

In some febrile diseases the urine, besides serving as a channel of excretion for toxins, contains also the organisms causing the disease. This is not uncommon, for instance, in typhoid fever; and it is probable that in all diseases where the organisms circulate freely in the blood-stream they may be detected in the urine.

In some febrile diseases, more especially in pneumonia and in cases of suppuration, such as empyema and cerebro-spinal meningitis, albumoses are present in the urine in comparative abundance, but rarely alone, serum albumin and globulin being also present. The albumoses are formed in the exudation produced at the seat of the disease; for instance, in the solidified lung of pneumonia, or in the purulent exudation of empyema, they are absorbed by the blood and are carried to the kidney, where they are excreted.

(*c*) Albuminuria of renal disease.—In Bright's disease the albuminuria is due to the damage and the shedding of the renal epithelium in the glomeruli and tubules. Some authors regard the change in the kidney structures as primary and brought about either by vascular changes, as in Bright's disease due to cold, or by toxic agencies, as in the Bright's disease due to alcohol, and in the sequel of acute specific maladies such as scarlet fever and pneumonia. Others look upon many forms of Bright's disease as being due to a disease of the blood, and hold that the kidneys are affected secondarily to this blood change. However this may be, the immediate cause of the albuminuria is the anatomical change in the renal epithelium.

Even in renal cirrhosis, where the albuminuria has been attributed to the high blood-pressure, it is more probably due, perhaps, to the accompanying epithelial lesions; for although the main lesion is in the interstitial tissue, yet in this disease there are always considerable tubular and glomerular changes.

In renal disease the actual amount of proteid matter found in the urine varies within very wide limits, being least in renal cirrhosis where there is sometimes but a trace, and rarely more than a few grammes in the twenty-four hours. On the other hand, in some forms of chronic Bright's disease, and in certain forms of lardaceous disease of the kidney, the amount may reach forty grammes a day. In acute Bright's disease, although the percentage of proteid matter in the urine is high, the amount lost is not very great, owing to the small amount of urine secreted. In the small white contracted kidney the amount of albumin lost is often considerable, amounting not infrequently to as much as twenty grammes daily. In diseases of the pelvis of the kidney, as in calculous, septic, or tuberculous pyelitis, the albumin in the urine, from the mere presence of pus or blood in the urine, is often considerable, and it is often of great moment to determine whether the albuminuria be due merely to the products of the pyelitis, or whether there is coexisting renal disease. In the latter case the amount of albumin in the urine may still be considerable after the pus or blood has been removed, either by subsidence or by the centrifuge. Again, if the albumin be of renal origin the urine will probably contain renal casts. In all such cases, however, the pus, blood, and other impurities should be removed from the urine before the latter is tested for albumin.

In renal diseases the proteids are usually present as a mixture of serum albumin and serum globulin. Sometimes albumoses are present, and occasionally, in renal cirrhosis, in large quantities, and serum albumin and serum globulin are present in traces only, so that if the urine is tested in the ordinary way by boiling, the presence of a large amount of proteid matter may be overlooked.

These cases of albumosuria in renal disease are rare, and their nature and cause are obscure, since the presence of considerable quantities of albumose in the urine is usually the result of absorption of the albumose from some inflammatory exudation into the blood; but in renal cirrhosis the albumosuria occurs without the presence of any inflammatory complication. It is possible that the albumose may be derived from the intestine.

Albumosuria occurs most frequently in cases of pneumonia and empyema; or, indeed, whenever there is a large collection of pus in any part of the body. The mechanism of the albumosuria in these cases is simple, inasmuch as albumoses are abundant in the inflammatory exudation, whether it be pus or the fibrinous exudation of the pneumonic lung. Some of the albumose present in the exudation is absorbed into the general blood-stream, and is thence excreted by the kidney just as it is after the experimental injection of albumoses intravenously.

Proteid tests.—The ordinary tests in use for the recognition of proteids in the urine are (α) the heat test; (β) the cold nitric acid test (Heller's test); (γ) the picric acid test; (δ) the copper sulphate and caustic potash test; (ε) the salicyl-sulphonic acid test.

(*a*) The heat test is perhaps the one most commonly used, inasmuch as it is simple, open to few fallacies, and fairly delicate. In performing this test the reaction of the urine must be previously ascertained; and, if necessary, it should be rendered faintly acid with acetic acid before boiling. Some authors prefer to add the acid after boiling; but it is probable that in this way small quantities of proteid matter may be overlooked. If the urine is not acid at the time of boiling, the proteid matter is liable to be converted on heating into alkali albumin, which is not coagulated by heat, and thus the presence of small quantities of proteid matter may be overlooked. It is no less necessary to avoid over-acidity of the urine, for in such urine, particularly if rendered acid with a strong mineral acid, the proteid coagulated may subsequently be redissolved. The principal fallacy in the heat test, however, is the precipitation of phosphates on warming faintly acid or neutral urines. This cloudiness is usually distinguished from the precipitated albumin by the particulate form of the latter: further, the phosphatic cloud disappears instantly on acidification; the proteid precipitate, on the other hand, does not.

(*β*) The cold nitric acid test.—This is an excellent test, if properly performed; but it is not quite so delicate as the heat test. The nitric acid must be pure, and, after being placed at the bottom of the test-tube, the urine to be tested should be floated on its surface with a pipette. If proteid matter is present in abundance, a ring is formed at once. If the amount is small, the ring only appears after standing. The fallacies of this test are as follows:—Proteid matter, if present, may be missed if the urine and the nitric acid are mixed up; hence nitric acid causing any effervescence of the urine, owing to the presence of nitrous acid, is not suitable for this reaction. Proteid matter, even if not present, may be suspected if a crystalline deposit of nitrate of urea be formed at the junction of the urine and the acid; this deposit is more apt to occur in concentrated urines, and the mistake is easily avoided by noting that the ring is crystalline in appearance. Occasionally mistakes arise from the formation of a dense highly-coloured ring at the junction of the urine and the acid. This ring (see Pigments of urine) is due to the formation of pigment from a chromogen present in the urine: it is coloured and not particulate; the proteid ring, on the other hand, is white and particulate.

By the nitric acid the presence of albumoses can be detected, bodies which are not brought into evidence by heat. Albumoses, and especially hetero-albumoses, which are the kind commonly present in the urine, form a precipitate on the addition of nitric acid. In testing for albumoses it is often better to add the nitric acid drop by drop to the suspected urine rather than to float the urine on the nitric acid. The characteristic reaction of albumose, however, is that the precipitate, formed by nitric acid, dissolves on heating, to reappear on cooling. The reaction is so characteristic that it may even be possible, although not advisable, to carry out the test in the presence of other proteid matter; as under these circumstances, if the quantity of albumose present be considerable, the coagulum produced by the nitric acid will diminish in amount on heating, to increase again on cooling. It is better, however, to remove the serum albumin and serum globulin, either roughly by heating, or by precipitation with some neutral salt, before testing the filtrate for albumoses with nitric acid.

Many resinous bodies after their administration are excreted in the urine, and these substances, on the addition of an acid, yield a precipitate that may be mistaken for albumin. This is especially true of copaiba and of oil of turpentine. The precipitate can be distinguished from proteid by its solubility in alcohol; but the addition of alcohol to nitric acid may cause an explosion.

(γ) *Picric acid.*—A cold saturated solution of picric acid is a useful test for proteids, and it has the advantage that it can also be used in testing for sugar. The addition of picric acid to a urine containing proteids is followed by the formation of a cloudiness or a copious precipitate, according to the amount of proteid matter present. From a clinical point of view the only serious objection to the picric test is that, in the first place, mucin is precipitable as well as ordinary proteids; and, secondly, that, as a proteid test, it errs on the side of delicacy: quantities of proteid are discovered by it which, at any rate, are of no serious clinical importance.

Picric acid is the agent that is more especially used in the investigation of cases of so-called physiological or functional albuminuria.

(δ) *Copper sulphate and potash.*—Copper sulphate and potash are reagents sometimes used in testing the urine, and the value of these lies in the fact that, whereas this test yields a rose colour with albumoses, it gives a violet colour with ordinary proteids; in fact, for the detection of small quantities of albumoses this test is, on the whole, preferable to the nitric acid test.

(ε) *Salicyl-sulphonic acid.*—This reagent is intermediate in delicacy between Heller's test and the heat and acetic acid test. A cold saturated solution of salicyl-sulphonic acid in water is used, and is added to the suspected urine in the quantity of one to three drops; however, an excess of the reagent does not interfere with the test. The fluid is then well shaken.

An immediate precipitate betokens the presence of an appreciable amount of proteid. If the precipitate does not fall in from one to two minutes the quantity of albumin is minimal; and if an interval be allowed to elapse, the test is really more delicate than the heat and acetic acid test. Normal urines give no precipitate with this reagent. This test is also of use for recognising albumoses and peptones, inasmuch as with these substances precipitates are obtained which dissolve on heating and reappear again on cooling.

Salicyl-sulphonic acid does not give any precipitate with bile salts, with urates, with alkaloids, nor with urine containing copaiba resin. With a large amount of mucin, however, a small amount of precipitate is obtained. This test is one not as yet in general use, but it is well worth the attention of clinicians.

Sometimes it is necessary not only to detect the various proteids present in the urine, but also to determine the relative quantities present. For this purpose the proteids must be precipitated with neutral salts; by saturating the urine with ammonium sulphate all proteid matter except true peptones are precipitated. On the other hand, magnesium sulphate is used to precipitate serum globulin alone, as it does not cause any precipitation of serum albumin or of albumoses. When the salts are used to precipitate proteids from the urine it is of course necessary to wash the precipitated proteid on the filter-paper with the saturated solution of the salt used. Thus, a precipitate of albumose obtained with ammonium sulphate must be washed with a saturated solution of ammonium sulphate. At the present time the precipitation of proteid matter in the urine by these solutions of neutral salts is used more for the purpose of research than of clinical routine.'

Quantitative estimation of proteid.—For rough estimations the amount of precipitate deposited at the bottom of the test-tube in twenty-four hours after heating and acidification with acetic acid is usually sufficient. This rough method, however, is liable to considerable error, owing to various conditions of the urine, such as its acidity for example, influencing the retractility of the coagulum.

If this method is employed, the amount of proteid is usually expressed in a fraction of the volume of the urine. A more accurate method is that of Esbach, where the urine is precipitated by a solution containing picric acid, and the amount of proteid is determined by the bulk of the deposit precipitated in a specially graduated tube. Esbach's method, although more accurate than the previous one, is open to a similar fallacy; and the only really accurate method is to precipitate the proteid and, after washing and drying the precipitate, to weigh it. The most convenient method of doing this, if the urine contain a considerable amount of proteid, is to add 5 c.c. of the urine to some 50 c.c. of boiling absolute alcohol. The mixture is allowed to remain in a hot-air oven at 80° C. for some hours, the precipitate is collected on a weighed filter-paper, washed with alcohol, ether, and water to remove the salts and fats, dried in the hot oven at 120° C. and weighed; if further control is desired, the total nitrogen in the precipitate can be determined by Kjeldhal's method.

Pyuria.—Pus may be present in the urine as the result of diseases of the urinary tract; as in suppurative nephritis, pyelitis, cystitis, or urethritis, or from rupture into the urinary tract of an abscess outside it, as in perinephritic or prostatic abscesses; or, finally, the urine may contain pus by simple contamination with a pus-secreting surface, as in cases of vaginitis. In all cases of pyuria it is important first to see the urine passed, and, secondly, to have it passed in at least two portions. In this way it is possible to separate the cases where the pyuria is of renal origin from cases of pyuria of urethral origin. Further, it is very important to separate the pus from the urine either by subsidence or, preferably, with the centrifuge before testing the supernatant clear urine for albumin. In this way it is possible to determine with certainty the presence or absence of organic renal disease in relation to the disease causing the pyuria. In cases of calculous pyelitis it is not uncommon for serious renal disease to be present in addition to the pyelitis. Abscess of the kidney, with or without perinephritic abscess, and pyelitis, leading to pyonephrosis, may be and frequently are present without the urine containing any pus. In fact, the absence of pus from the urine is a matter of comparatively small importance in the diagnosis of pyonephrosis in the presence of a renal tumour. Pus present alone in the urine, unless the amount of it be very large, does not cause more than a trace of albumin. Hence the appearance of a considerable amount of albumin in the urine containing pus is always suggestive of the coexistence of renal disease. The presence of casts containing renal elements will also assist us in forming this diagnosis. Urine containing pus may be acid or alkaline; the former is more characteristic of the pyuria of renal origin, the latter of that of vesical origin.

If, however, cystitis be slight in amount the urine may remain acid, as in some cases of pyelitis; on the other hand, in pyelitis complicated with cystitis the urine may be alkaline. Hence, in the differential diagnosis, too much stress must not be laid on the reaction of the urine. In acid urine the pus corpuscles are discrete and subside; in alkaline urine the pus is ropy and stringy. Pus is best recognised by microscopical examination, but the suspected urine, if acid, may be tested by the addition of liquor potassæ, which causes any purulent deposit to become ropy. Ozonic ether causes an effervescence in urine containing pus.

Glycosuria.—The normal urine contains several reducing substances, and there has long been a difference of opinion whether these reducing substances are only urates or kreatinin, or whether traces of sugar are also present. Now, however, it is admitted that the normal urine contains carbohydrate material, at any rate in the form of glycuronic acid; and that the whole of its reducing power, therefore, is not to be attributed to the presence of urates and kreatinin. It is possible, but not certain, that a very small amount of dextrose is also present; but even if this be so, which is doubtful, the quantity is so small as only to be detected after concentration of large volumes of urine; hence, if present, it is of no clinical importance.

Glycosuria is not infrequently seen without the other accompaniments of diabetes. Thus it occurs in certain circumstances in the apparently healthy; and to this the name of *functional glycosuria* has been applied, analogous to that of the so-called functional albuminuria described above. Traces of sugar appear in the urine in certain persons after severe exercise; in others, and a much larger group, after meals, and more particularly, perhaps, after meals rich in carbohydrates. The ingestion of large quantities of milk is not infrequently followed by the presence of reducing substances in the urine, probably lactose. In the cases where glycosuria is observed after meals, a state which has been called "dietetic glycosuria," the patients not uncommonly have gouty manifestations also. They are often obese, and hence the name "lipogenic glycosuria" has been used in these cases. It is very probable, however, that no hard and fast line can be drawn between diabetes on the one hand and these cases of more or less temporary glycosuria on the other.

Glycosuria, slight in amount, is frequently seen in certain grave diseases; and more especially in diseases leading to increased intracranial pressure, such as meningitis, cerebral hæmorrhage, and cerebral tumour. This is more especially the case in infra-tentorial disease, and in disease about the medulla oblongata. It is not limited to these cases, however, and may be present in cases of cerebral hæmorrhage in the ordinary situations; namely, in the external capsule and in ventricular hæmorrhage. Glycosuria also occurs after injuries to the head and in epilepsy.

It is rather remarkable that sugar does not appear in the urine in cases of hepatic cirrhosis and in acute yellow atrophy; more particularly so if we regard the liver as a "sugar-stopping" organ. On the other hand, if the liver be a sugar-forming organ, this result would not be surprising after the extensive destruction of the liver that occurs in these diseases.

Glycosuria is also said to occur after the administration of various drugs and poisons, more especially of morphia, chloral, opium, chloroform, and carbonic oxide. It is probable, however, that the reducing substance in the urine is not dextrose, but a compound of glycuronic acid. This is certainly the case after the administration of chloral. Slight glycosuria is also stated to occur in cases of cardiac and pulmonary diseases, leading to venous congestion of the kidney; and it has occasionally been found transitorily in various acute specific diseases.

The sugars met with in the urine are dextrose, lactose, and inosit, very rarely lævulose; and the last is rarely present alone, as dextrose usually accompanies it. Lævulose, lactose, and inosit are, however, of no great clinical importance. It is asserted by some authors that traces of dextrose are present in the normal urine; but, as I have said already, special methods are necessary for its detection; and it is probable that the slight reducing power of the normal urine is dependent mainly, if not entirely, on the presence of kreatinin, urates, and compounds of glycuronic acid. Benzoyl chloride is an agent that can be used for the precipitation of carbohydrate material in the urine, and it has been shown that normal urine contains carbohydrate derivatives; but there is no evidence of the presence of dextrose in any quantity. The blood normally contains 0·05 to 0·09 per cent of sugar; and when the proportion of sugar present rises to some 0·3 per cent this substance appears in the urine. The amount of sugar passed in the urine in diabetes mellitus varies from an ounce or two to as much as a pound or a pound and a half in twenty-four hours; occasionally even greater quantities may be passed for a short time, and as much as one pound a day may be passed daily for considerable periods. The percentage of sugar in the urine rarely, if ever, rises above 10 per cent; and it is uncommon for it to reach this high limit, since the excretion of large quantities of sugar always causes a great increase in the amount of urine passed. In diabetes mellitus the quantity is usually considerable and sometimes enormously increased; thus, 5 to 10 pints a day are quite ordinary amounts for a case of moderate severity; and the quantity may be increased to 15 or 20 pints, but this is exceptional. When the quantity is increased to some 5 to 10 pints the urine is of a pale greenish yellow colour. Sometimes the quantity is but slightly increased, and, here the urine retains its normal colour; but the quantity of sugar present in these cases is necessarily not very large since, even if the percentage of sugar be high, the amount of urine is not sufficient to lead to a great loss of sugar. Glycosuria without polyuria is perhaps more often seen in the less severe cases of diabetes in the aged, and in the cases of so-called gouty glycosuria. These cases are liable to be overlooked, as the patient very frequently does not suffer from thirst. The specific gravity of urine containing sugar is usually high. A specific gravity of 1025 or above in a pale-looking dilute urine suggests the presence of sugar; and a specific gravity above 1035 in such a urine is almost always due to sugar. The specific gravity does not vary, however, directly and proportionately with the amount of sugar present. Sugar may be present in the urine when the specific gravity is as low as 1010. It is possible, however, that some of the cases described as cases of glycosuria with a low specific gravity have really been cases in which glycuronic acid was mistaken for dextrose.

In diabetes, other abnormal constituents of the urine, such as diacetic acid, acetone and oxybutyric acid, are usually present with the sugar. Diacetic acid is the one most frequently present. These bodies, especially diacetic acid and acetone, are present in the urine in cases of diabetes even when no symptoms of acetonæmia are present. In diabetic coma, however, they are usually much increased in amount, and recent observations have shown that in a large number of cases of diabetic coma β-oxybutyric acid is present in the urine in comparatively large quantity.

The amount of sugar in the urine in diabetes is not only variable but not uncommonly fluctuates greatly in the daily excretion, quite apart from any influence of treatment. Thus, in febrile complications occurring in the diabetic the amount of sugar may diminish or even disappear entirely. Further, in diabetes, it is not uncommon for sugar to disappear suddenly and completely from the urine. In many of these cases coma is imminent, but this is not invariable; the urine may remain free from sugar for a few days, and then contain it again in its former abundance.

The cause of these fluctuations, and still more of the sudden and spontaneous disappearance of sugar, is very obscure. In diabetic coma the sugar almost always undergoes a diminution, and not uncommonly disappears; hence the gravity of a sudden and great diminution in the amount of sugar passed. In diabetic coma, with the diminution or the disappearance of the sugar, the quantity of urine also undergoes great diminution. In many cases of diabetes albumin appears in the urine towards the end; and, if the amount of albumin be large, the Fehling reaction does not take place satisfactorily unless the albumin be previously removed; therefore, in testing highly albuminous urines for sugar the albumin should always be removed before the sugar test is applied. The presence of albumin, however, does not prevent the success of the sugar test unless the amount of it be large. The well-known odour of diabetic urine is dependent on the presence of diacetic acid and acetone, more frequently on the former than on the latter. When in diabetic coma the sugar disappears or undergoes diminution, the diacetic acid and acetone are increased in amount; and although these bodies are almost always excreted abundantly in diabetic coma, their presence in the urine is not restricted to this condition.

Sugar tests.—In testing the urine for sugar many precautions are necessary. Fehling's solution must be freshly prepared, or care taken that it has not undergone decomposition. The urine should be added in a small quantity to an excess of boiling Fehling's solution. If a considerable quantity of sugar be present, a few drops of urine are sufficient to yield the characteristic reaction. If only a small quantity be present, a larger quantity of urine, amounting to a half or at the most an equal volume to that of the Fehling's solution, must be used. Excess of urine and prolonged boiling are both to be avoided, especially if the urine is a concentrated one; as, under these circumstances, the reduction of the copper by urates or kreatinin may be attributed to sugar. If copper sulphate and potash are used instead of Fehling's solution it is necessary not to have an excess of copper present; since, if the amount of sugar be small, some black oxide of copper may be formed and may obscure the formation of the red oxide.

When the reaction is doubtful the reduction occurs only after prolonged boiling; or a yellowish green discoloration is obtained instead of a brick-red precipitate. Under these circumstances it is not safe to regard sugar as present without the application of some corroborative test. Of these, one of the simplest is the fermentation test, and this has the further advantage of distinguishing glycuronic acid from sugar. As a test for the presence of sugar, fermentation is excellent; but it is not so valuable for its quantitative estimation.

To perform the fermentation test a small quantity of mercury is placed in a test-tube filled up with urine, to which a fragment of yeast has been added. The test-tube is then inverted in a small vessel containing mercury and kept for some hours at the temperature of the body, preferably in an incubator. The test is said to be sufficiently delicate to reveal the presence of 0·1 per cent of sugar.

The phenyl-hydrazin test.—This test is of value, both from its delicacy, and that by its use sugar may be recognised in its different varieties. It depends upon the fact that phenyl-hydrazin with glucose forms crystalline needles, which are but slightly soluble in water. Hydrochlorate of phenyl-hydrazin and acetate of soda are mixed together in the proportion of two parts of the former to three of the latter, and to the mixture some 10 c.c. of urine are added. The fluid is then warmed by placing the test-tube in a water-bath for half an hour. On cooling, should sugar be present, a distinct crystalline deposit is formed, which under the microscope is seen to consist of needles. If the urine contain a large quantity of albumin it is better to remove it before applying the test.

The picric acid test.—A few drops of saturated solution of picric acid are added to the urine, to this is added caustic potash, and the mixture warmed. The presence of sugar determines a deep red colour. This test has the advantage that it can be performed in the presence of albumin; but it has the great disadvantage that a somewhat similar colour, though not of the same depth, is yielded by kreatinin: by itself, therefore, the test is not conclusive of the presence of sugar.

Glycuronic acid.—This acid is frequently present in the urine in appreciable quantities, and probably traces of it are normally present. It is especially abundant in the urine after the administration of certain drugs, more especially chloral and camphor. As mentioned above, in cases of indicanuria the quantity of glycuronic acid is considerably increased, since the indol and skatol formed in the alimentary canal appear in the urine in part as compounds of glycuronic acid. This acid is of carbohydrate origin, and, as it reduces Fehling's solution, it is liable to be mistaken for sugar. It is said that some of the cases where sugar is supposed to be present in urine of low specific gravity are really instances of excessive excretion of glycuronic acid. This body, although reducing Fehling's solution, does not yield carbonic acid on fermentation. Glycuronic acid itself is dextro-rotatory, its compounds are lævo-rotatory, and it forms with phenyl of hydrazin a compound which melts at 115°; whereas the corresponding compound formed with dextrose melts at 205°.

Acetone.—Acetone is found in the urine in many conditions, as in diabetes mellitus, febrile diseases, and the cachexia of malignant disease. It is stated to occur in starvation, and also after anæsthesia; but, according to Abram, neither the quantity of anæsthetic used nor the duration of the anæsthesia has any well-marked effect on the amount of the acetonuria; it is stated that acetonuria occurs in at least two-thirds of the cases of anæsthesia. Acetone is also stated to occur in traces in the urine in health, and more especially in children. In diabetes mellitus acetonuria alone is certainly not indicative of the presence or imminence of diabetic coma. Acetone is the cause of the peculiar etherial odour often noticed in cases of diabetes, both in the urine and the breath.

In diabetes acetonuria is frequently accompanied by the presence of diacetic acid; and some of the so-called tests for acetone depend really on the presence of diacetic acid. If the amount of acetone in the urine is small, it can only be recognised by distillation; if large, one or more of the following tests may be used:—The suspected urine is added to a solution of iodide of potassium in liquor potassæ, and the liquid boiled; if acetone be present, crystals of iodoform are formed. A convenient strength of the solution is 20 grains of iodide of potassium to a drachm of liquor potassæ.

Another test for acetone is that of Legal. To the suspected urine a concentrated freshly-prepared solution of sodium nitro-prusside and some caustic soda are added. A red colour is formed, which disappears, and on the addition of acetic acid is replaced by a purple. Diacetic acid is recognised by the red colour which it yields with ferric chloride.

β-Oxybutyric acid occurs in the urine in diabetes, and more especially in diabetic coma. It is, however, seen in febrile states also. There is no convenient test for this substance, but it may be recognised by fermenting the urine with yeast, filtering, concentrating, and distilling the filtrate with concentrated sulphuric acid. α-Crotonic acid separates from the distillate on cooling, and may be recognised by the fact that the crystals melt at 72°.

B. The Kidneys

Physiological considerations.—The kidneys share with the skin, the lungs, and the intestines the duties of eliminating from the body substances, either produced in the course of metabolism or introduced from the outside, which are either no longer useful or positively injurious.

In health the excretion of the urinary pigments may be instanced as illustrating the former, and the various nitrogenous extractives and salts as illustrating the latter. In disease, the removal of sugar in diabetes illustrates the excretion of a substance no longer useful; and the toxins excreted in the urine in microbic diseases afford an illustration of substances injurious to the economy. In the course of this process in health a considerable quantity of water is eliminated by the kidney; approximately 50 per cent of the quantity ingested. The great bulk of substances excreted in the urine are formed in other parts of the body, and the kidneys are only concerned in their removal from the blood-stream. Some constituents of the urine are, however, undoubtedly formed in the kidney.

The functions of the kidney may be classified somewhat as follows:—

(i.) The excretion of water.
(ii.) The excretion of salts, pigments, extractives.
(iii.) The synthesis of some constituents of the urine.
(iv.) The metabolic activity.

1. The excretion of water.—The excretion of water by the kidney is intimately related to the state of the circulation in the kidney, and as yet there is no definite experimental evidence of any kind of influence of the nervous system on the water excretion, except the indirect one exerted through the vaso-motor system.

Broadly speaking, the elimination of water depends on the rate of the flow of the blood through the glomerular tufts, and most substances normally present in the urine, when introduced into the circulation, bring about a dilatation of the renal blood-vessels. Some substances, however, such as digitalis, cause an increased flow of urine, notwithstanding that they produce constriction of the renal vessels. This, however, is dependent on the fact that, along with the renal constriction, there is general vascular constriction; and the heightened blood-pressure so produced causes an increased flow of blood through the kidney. In pathology it is important to bear in mind that the rate of the flow of blood through the kidney is of more importance in determining the actual amount of water excreted than the actual blood-pressure. Although there is no definite proof of the existence of renal nerves apart from vaso-motor nerves, yet it is possible, if not probable, that such exist. Many operative procedures, such as the placing of a canula in the ureter, bring about complete arrest of the urinary secretion. It is difficult to suppose that this is due to a vascular effect, as oncometric observations do not show that such operations produce any direct and sudden effects on the volume of the kidney.

Some observers have thought that the kidney reabsorbs water; in other words, that the urine, as secreted by the glomeruli, is more dilute than that passed out from the renal pelvis; and the facts of comparative anatomy as regards the structure of the kidney in different animals are appealed to in support of this opinion.

The amount of water excreted apparently depends also on the amount of kidney substance. This conclusion is based upon the consideration of the following facts:—If a portion of one kidney be excised, the operation is followed by an increase in the amount of urinary water. This increase is not seen after simple incision and suture of the kidney; to produce it a portion must be removed, although the effect is seen when the portion removed is small, weighing perhaps but a few grammes. If, after the removal of a portion of one kidney, the second kidney be also removed entire, leaving the animal with less, therefore, than one kidney, the increase in urinary water is very considerable, amounting frequently to twice the normal quantity. No other profound effect is seen, provided the amount of kidney left approximates to one-third of the previous total normal kidney weight. This increase in urinary water, as far as my observations go, is a permanent one; at any rate it persists for periods of four to six months. The removal of a wedge from each kidney produces a very great increase in urinary water, often greater than that seen in the previous series of experiments. In some cases the flow has been quadrupled. This condition is also very persistent, but is not followed by any marasmus or marked deterioration in the health of the animal; the only striking phenomenon being the abundant dilute urine, approximating in character to that seen in the human subject in cases of renal cirrhosis and diabetes insipidus. No cirrhosis or interstitial inflammation of any kind is induced in the organ as the result of these excisions; therefore the increase in the urinary water is in no way dependent upon any secondary pathological process started in the kidney by the operation. Apparently no such increase ensues on removal of one entire kidney. Division of the renal plexus is not followed, so far as my observations go, by any permanent increase in the urinary flow; and division of the renal plexus has no influence in modifying the results produced by the excision of portions of the kidney. It is immaterial in such experiments whether the renal plexus be divided or not.

I am not prepared to offer any explanation of the increased urinary flow, but it is possible that the partial ablation of a kidney produces secondary effects on the blood-pressure, and that this is raised. It is also possible that there is a greatly increased rate of flow through the fragment of kidney left, and that in this way the elimination of water is increased. It is also possible, but not probable, that the increased flow depends on a diminished reabsorption of water; but the fact that the greatest and most marked effects are seen after partial bilateral nephrectomy is in favour of the dependence of the phenomenon on some secondary effects produced on the vaso-motor system.

The kidney is enormously vascular, and is one of the most useful organs in the body for the investigation and demonstration of vaso-motor phenomena.

The kidney in animals (dog) receives its vaso-motor nerves from the sixth dorsal nerve to the third lumbar inclusive; that is to say, from a consecutive series of eleven nerve-roots, inasmuch as the dog has thirteen pairs of dorsal nerves. It is, however, only the lower of these nerve-roots that contain an abundant supply of vaso-motor nerves. Although the great bulk of nerves distributed by these roots are vaso-constrictor nerves, yet there is definite experimental evidence that the lower dorsal and upper lumbar roots contain some vaso-dilator fibres. Further, the kidney receives from the posterior roots a number of afferent nerves, the excitation of which, by producing constriction of large vascular areas, causes a very great increase of the general blood-pressure. It is remarkable that nerves, the excitation of which causes a fall of blood-pressure by bringing about general dilatation, for example, the depressor nerve, the central end of the lower intercostal, etc., do not produce any marked direct fluctuations in the volume of the kidney.

ii. The excretion of salts, pigments, etc.—Although these are grouped together, they are excreted by different portions of the kidney; thus the salts—and certainly the abnormal pigments—are excreted by the glomeruli: the urea, on the other hand, is removed by the tubules. The urea is definitely known not to be formed in the kidney, but simply to be removed. The blood normally contains (approximately) 0·015 per cent, and thus the selective activity of the renal epithelium may be gauged, inasmuch as the urine contains approximately 2 per cent of urea. Although the renal epithelium has such marked selective affinity for eliminating urea, the kidney is able to remove a number of substances introduced into the general blood-stream, especially when such substances are abnormal constituents; but, on the other hand, it will also eliminate normal constituents of the blood-stream not usually present in the urine in cases of a marked increase in such substances. Thus the abnormal presence of albumoses in the blood is followed by their prompt excretion by the kidney. The same applies to the presence of bile pigments in the blood. A normal constituent of the blood, like sugar, which is probably not normally present in the urine, appears readily in this fluid when the percentage in the blood increases from the normal 0·09 per cent to 0·3 per cent. Nothing demonstrates the selective activity of the renal epithelium better than the fact that, although there is in the blood some four or five times as much sugar as there is urea, the urine contains either no sugar or traces at most; whereas, as mentioned above, the percentage of urea is at least one hundred times greater than in the blood. Although most of the constituents of the urine are derived either from the products of the metabolism of the tissues, or from the ingestion and absorption of various food constituents, some of the urinary constituents reach the urine by a roundabout course; thus the aromatic sulphates of the urine are derived principally from the decomposition of proteid matter in the intestine, and it is certainly remarkable that these substances should be absorbed from the intestine and subsequently excreted by the kidney. Hence the eliminating functions of the kidney are not only related to those of the skin, but are in connection with the intestine also; so that it is quite conceivable that, if the eliminating functions of the kidney should be seriously impaired, an accumulation of more or less toxic materials might occur in the intestines; and this independently of the fact that when the urinary flow ceases, urea, and probably other bodies, are excreted by the mucous membrane of the stomach and the bile.

Most substances readily excreted by the kidney produce at the same time a copious flow of urinary water, and oncometric observations show that such substances produce vascular dilatation of the kidney.

iii. The synthesis of some of the constituents of the urine.—The urine contains traces of hippuric acid. In many animals the quantity is considerable. In man the quantity is greatly increased as the result of the ingestion of substances containing benzoic acid or its compounds. It is definitely known that when benzoic acid is ingested, it is excreted as hippuric acid, and that the conversion of benzoic into hippuric acid occurs in the kidney. This fact is important, as showing that the kidney is capable of synthesising complex organic substances; and what is true of hippuric acid may be true for other urinary constituents.

It has recently been asserted (Luff) that uric acid is formed in the kidney and not, as is more commonly believed, in the liver or spleen. This conclusion is largely based on the difficulty of determining the presence of uric acid in the blood, even in the cases of animals, such as birds, whose urine contains large quantities of uric acid. The blood of such creatures has long been known to contain urea (Garrod), and it has been supposed that the kidney is concerned in the conversion of urea into uric acid. The removal of the liver in such animals, however, is followed by a very great diminution in the uric acid excreted, and most physiologists consider that this fact points to the conclusion that the liver is the organ in which the uric acid is formed. Further, the removal of the kidneys in birds, or their destruction by repeated injections of bichromate of potash (Ebstein), is followed by the deposition of uric acid in various tissues and organs of the body.

iv. Metabolic activity.—Recent physiological observations have shown that the suprarenal, thyroid, and pancreas are glands possessing internal secretions; and a series of observations have been made by myself to see whether the kidneys possess any such functions. The object of these experiments was, by diminishing the amount of kidney substance, to observe whether the resulting phenomena were due to a deficiency in the excretory function of the kidney. The general result of these observations was as follows:—The removal of a portion of one kidney is not followed by any permanent after-effects, except in the case of the flow of urinary water. The removal of a portion of both kidneys produces the same excessive flow to a greater amount. The removal of a portion of one kidney and the whole of the other, again, is followed by the same effect, provided the quantity of kidney left amounts to not less than one-third of the previous total kidney volume. The removal of a portion of one kidney and of the whole of the other is followed by death, if the amount left is, approximately, no more than one-fourth of the total normal kidney weight. The period of survival after this last operation is very short—rarely more than three weeks, sometimes as short as one week. In this last series of cases, not only is the quantity of urine greatly increased, but there is also an increased excretion of urea, absolute or relative; by the former is meant that the actual amounts excreted are greater than those previously excreted on a full diet in health. By the term "relative increase" is meant a condition in which the excretion of urea remains at the height at which it existed previously on a full diet, notwithstanding that no food is taken subsequently to the operation. In other words, if the animal refuse food, as sometimes is the case, the amount of urea excreted equals that previously excreted on a full diet; whereas if the animal eat, the amount of urea excreted is increased. This increased excretion of urea is accompanied by great wasting, especially of the muscles, and great consequent weakness. The marasmus is accompanied by a great fall of the body temperature. The blood and tissues contain a large excess of urea and other nitrogenous extractives at a time when the increased excretion of urea is in full swing. When the animal is moribund the increased excretion of urea and urine diminishes. I think it is clear from these observations that the removal of very large quantities of kidney substance—that is, over three-quarters of the total kidney weight—is followed by a disordered metabolism of such a character that the production of urea is increased; and that the increased urea and nitrogenous extractives present in the blood and tissues are dependent on this increased production, and are in no way caused by any deficiency in the excretory activity of the kidney.

It is most remarkable to see how these fragments of kidney will excrete quantities of urine and urea far greater than those normally excreted from two intact kidneys. The disordered metabolism produced by these extensive partial nephrectomies is in no way due to a disturbance of the nervous system produced by mutilation, since the division of the renal plexus has no influence in moderating or increasing the severity of the effects, and the phenomena are dependent entirely on the quantity of kidney substance removed at the operation, and not on the mutilation produced in removing it. Thus a greater quantity of kidney is removed by excising a wedge from one kidney, and subsequently removing the whole of the second kidney, than by removing a wedge from each kidney; yet the mutilation and severity of the operation are far greater in the latter case than in the former. The latter operation is never followed by an increased urea excretion; the former may be if the quantity of kidney removed is some three-fourths of the total kidney weight. These observations point to the existence of another function of the kidney apart from its excretory function; since the latter is, at any rate, not abrogated by the procedures, whereas the metabolism of the body is very seriously deranged. Whether this is dependent on the existence of an internal secretion I am not prepared to say, since such a conclusion is not justifiable until the disordered metabolism produced by the operation can be successfully arrested by the injection or administration of a kidney extract. As yet such experiments have not been carried out. Finally, whether the kidney possess an internal secretion or not, it is clear, I think, that the diminution in the amount of the kidney substance available produces a widespread disturbance of the general metabolism, in no way dependent upon the impairment of its functions as an excretory organ.

THE GENERAL PATHOLOGY OF RENAL DISEASE.—The pathology of diseases of the kidney may be divided into two series of phenomena: first, the pathological results of diseases of these organs; and, secondly, the mode of production of the diseases themselves.

Diseases involving the kidneys tend to produce one or more of the following pathological defects:—

1. Alterations in the composition of the urine; 2, œdema; 3, uræmia; 4, cardio-vascular changes; 5, marasmus and anæmia; and 6, liability to septic inflammations, that is, the so-called secondary inflammations.

1. Alterations in the urine.—The normal flow of urine depends upon the activity of the glomerular epithelium, and on the rate of the blood-flow through the vessels. The urinary flow is diminished as the result of morbid conditions affecting one or more of the following mechanisms:—

(i.) *Circulatory changes in the kidney.*—(*a*) *The direct action of various substances on the renal vessels.*—Substances acting on the renal blood-vessels may bring about a diminution in the quantity of urine, or even actual suppression, by causing vascular constriction. Frequently this constriction, even if extreme in amount, is followed by dilatation, depending in many cases upon damage to the vessel wall by the constricting substance, as by turpentine. Many substances which in certain doses cause constriction of the renal vessels, in other doses cause dilatation and diuresis; citrate of caffein is a striking example of this contrast.

Further, substances like caffein, which produce a double effect—constriction followed by dilatation, if given experimentally in rapidly repeated doses cause constriction only, and even complete suppression.

This action of substances on the renal vessels is a direct one, as shown by the fact that division of the renal plexus has little effect on the phenomena; and, further, that the characteristic effects can be produced in a kidney, excised from the body, through which an artificial circulation is maintained.

(*b*) *Indirect or reflex effects on the renal vessels produced through the nervous system.*—Constriction of the renal blood-vessels produced by reflex excitation is not so likely to lead to diminution or suppression of the urinary flow as direct excitation; since on reflex excitation the local effect is liable to be accompanied by a general constriction, and thus the flow through the kidney is not diminished to the same extent. It must be remembered, however, that substances acting directly on the blood-vessels have not, as far as we know, any special action on the renal vessels, and therefore, to a certain extent, the effects produced in both conditions will be similar.

Although constriction of the kidney is readily brought about by reflex excitation of the sensory nerves, it is doubtful whether complete suppression, lasting for any length of time, can be produced in this way. Stimulation and excitation of the central ends of the lower dorsal nerves produce reflex dilatation of the kidney, along with a general constriction.

(ii.) *Epithelial changes.* — (*a*) *The changes produced as a result of the above circulatory changes.*—Interference with the renal circulation, whether by the production of constriction or dilatation, is followed very quickly by changes in the renal epithelium; and these are undoubtedly largely responsible not only for variations in the amount of the urine, but also for alterations in its composition.

(*b*) *Direct toxic action of various substances on the epithelium.*—In many microbic diseases, more especially in diphtheria, anuria is not uncommon; and often in fatal cases there are no signs of any very profound lesions of the vessels of the kidney. It is probable that in these cases suppression is brought about by the action of the morbid poisons on the epithelial elements of the kidney. This is in striking contrast to the suppression seen in acute nephritis and scarlet fever, where the changes in the blood-vessels and circulation are very marked.

(*c*) *The action of the nervous system directly on the kidney cells and on the blood-vessels.*—This action must, at the present time, be considered purely hypothetical; yet a number of cases of complete suppression arise as a result of reflex excitation of some part of the nervous system. This suppression may last for days; and it is difficult to suppose that it depends entirely on reflex effects on the blood-vessels, since, as mentioned above, although it is possible, experimentally, to cause diminution in the flow of urine by the reflex stimulation of nerves, yet it is difficult to arrest the flow completely for any length of time.

An increased flow of urine is described above in the section on "Urine" as a characteristic phenomenon in many diseases. In some, as in diabetes mellitus, the mechanism is comparatively simple, inasmuch as the increased flow probably depends closely on the presence of the sugar, which is a powerful diuretic; it is not entirely due to this, however, as the increased flow may sometimes persist when the sugar is largely diminished. The kidneys in diabetes mellitus are usually considerably hypertrophied. In cirrhosis of the kidney the mechanism is by no means so clear. The increased flow here has usually been supposed to be dependent on the heightened arterial tension increasing the rate of flow through the remaining kidney substance. The increased flow cannot very well be due simply to increased blood-pressure favouring filtration, inasmuch as, physiologically, the flow of the amount of urine is not dependent upon the absolute blood-pressure of the renal vessels, but upon the rate of flow through the renal vessels.

The increase seen in renal cirrhosis is somewhat similar to the increase seen after the experimental removal of portions of the kidney; and it may perhaps be dependent rather upon the diminution in the available kidney substance than upon the increased blood-pressure. It is possible that the increase in the amount of urine may, to a certain extent, be an indication of the degree of destruction of the kidney substance. It is certainly remarkable how great are the quantities of dilute urine sometimes passed by kidneys with very advanced and general destructive and fibroid changes, a change so widespread and extensive that but little kidney structure may remain. In amyloid disease the increased flow is supposed to depend upon the increased permeability of the glomerular tuft. In chronic nephritis, in which the amount of interstitial change is frequently considerable, the flow is also increased; and here the cardio-vascular changes are often by no means so well marked as in cases of so-called granular kidney. It is difficult to say whether in these cases the increased flow is dependent simply on the increased blood-pressure, or whether here also it is related to the destruction of the kidney substance.

In chronic nephritis with dropsy the subsidence of the dropsy is always associated with an increased flow of urine.

The other abnormalities of the urine in renal disease are considered in the section "Urine."

2. **Dropsy** is a frequent accompaniment of renal disease, but the association is not an invariable one. Some diseases of the kidney never cause dropsy, and no disease of the kidney causes it always. Dropsy is peculiarly associated with Bright's disease, acute and chronic, but even in this malady its occurrence is not invariable, and acute Bright's disease of the greatest severity may occur without the presence of any dropsy. In other forms of this malady dropsy may be the most prominent symptom, and the severity of the lesion, as judged by the alterations in the composition of the urine, may not be any more severe than in cases unaccompanied by dropsy. Dropsy is most frequent in the cases of

Bright's disease dependent on scarlet fever, cold, and alcoholism. It is remarkably frequent in what is known as the large white kidney; not so common in cases of small white kidney. It is also frequent in the waxy kidney. The dropsy seen in certain cases of granular kidney is usually held to be associated with some accompanying cardiac lesion.

Dropsy does not occur in cases of suppression of urine from calculous obstruction, even when this lasts as long as a week or ten days. It is also uncommon in the partial or complete suppression seen in diphtheria; but dropsy does sometimes occur in this latter state. Slight dropsy is often seen in cases of eclampsia, but here it is probable that the dropsy is dependent on the coexistence of renal disease. Tuberculous and malignant disease of the kidney do not of themselves necessarily lead to dropsy.

Renal dropsy is associated with the diminution in the amount of urine excreted, so that an increase in the dropsy is always associated with a corresponding diminution in the amount of urine voided. And, conversely, an increased flow of urine is associated with a subsidence in the amount of the dropsy. Dropsy in cardiac disease is also associated with a diminution in the amount of water excreted, so that some observers have considered that so-called cardiac dropsy does not arise unless, owing to the venous congestion produced by the cardiac lesion, there is some interference in the rate of the blood-flow through the kidney, and hence a diminished excretion of urinary water.

In cardiac diseases, however, it is probable that the relationship is not one of cause and effect, but simply an associated defect; the increased venous pressure leading, on the one hand to anasarca, and on the other hand to the diminished excretion of urinary water.

The dropsy of renal disease affects more especially the subcutaneous tissues, and is most readily detected over the sacrum, the scrotum, the eyelids, and the shins. Not uncommonly the patient's attention is first attracted to the malady by the puffiness of the lower eyelids; œdema here, however, is by no means always due to renal disease. The dropsy affects also the serous cavities, and when the general œdema is at all marked there are dropsical accumulations in the serous cavities, more especially in the pleural cavities.

Œdema of solid organs, such as the lungs, brain and larynx, is also common; but pulmonary œdema is perhaps the most serious, and at the same time a very frequent complication of renal disease. Œdema of solid organs, and more especially of the lungs, is usually found in long-standing cases of renal dropsy, and pulmonary œdema is frequently associated with hydrothorax. Pulmonary œdema, however, is not uncommonly seen in fatal cases of uræmia, when there is no general dropsy. It is important to recognise that pulmonary œdema in renal disease is not always a mere accompaniment of general water-logging, but is a frequent, if not invariable, accompaniment of uræmia. Œdema of the glottis is by no means so frequent; and œdema of the brain, although sometimes very well marked, is likewise by no means an invariable accompaniment either of renal disease or of uræmia.

The fluid found in the serous cavities in renal disease is remarkable for containing only a small percentage of proteid; and that found in the subcutaneous tissue contains a still smaller percentage, frequently not more than one per cent. The amounts of proteid found in the dropsical fluids are far less than those seen in inflammatory exudations, or even than those found in the dropsical transudations of heart disease. Whether œdema be caused by cardiac or renal disease, the percentage of proteids present in the subcutaneous fluid is less than that seen in the fluids found in the serous cavities; but the amounts present in the transudations of renal disease are far below those seen in the transudations of cardiac disease. This is not surprising in renal disease, considering the continual loss of albuminous substances from the blood plasma, owing to the albuminuria.

The dropsy of renal disease is thus peculiar in its distribution, affecting mainly the subcutaneous tissues; and in its composition, owing to the small amounts of proteid matter present. The dropsical fluids in renal disease contain large quantities of nitrogenous extractives, more especially in uræmia; even when there are no signs of uræmia, the blood and dropsical fluids of a patient with Bright's disease contain a notable excess of urea and other nitrogenous extractives.

By an examination of the pleural and peritoneal fluids in cases of Bright's disease associated with dropsy, it is possible to determine, approximately, the amounts of nitrogenous extractives present in the blood. The dropsy of chronic Bright's disease conceals, to a great extent, the general wasting which occurs in this malady, and which becomes very apparent if from any cause the dropsy subside.

Dropsy is sometimes the first obvious sign of grave and unsuspected renal disease; both in acute Bright's disease, and in subacute Bright's disease of insidious onset. Cases of the general œdema characteristic of Bright's disease are sometimes seen, however, in which, on examination of the urine, no confirmation of this suspicion is found.

The causation of renal dropsy is obscure, much more so than in the case of cardiac dropsy; and many hypotheses have been advanced to explain it, none of which is wholly satisfactory. From a pathological point of view, the dropsical transudations found in renal disease are after all accumulations of more or less abnormal lymph—abnormal especially from the presence of a small amount of proteid matter and the large amount of extractives. The abnormality of the composition of the fluid, however, is most obvious in chronic cases, and can be accounted for fairly well by the fact that the blood itself is rich in extractives and poor in proteid constituents. The inquiry is therefore narrowed down to the actual cause of the increased transudations of lymph. An increased transudation of lymph must, as far as is known, be dependent ultimately either on primary alterations in the wall of the capillaries increasing their permeability, the blood-flow through them and the blood-pressure in them remaining normal, or else upon an alteration in the blood-pressure and blood-flow in the capillaries themselves.

Physiologically, it can be shown that an increased lymph-flow is readily brought about by any condition increasing the venous pressure, either general or in the locality affected. Some physiologists have held, however, that the capillary wall exerts a very special and selective action on the contained blood; and that, to a certain extent, the flow of lymph is to be looked upon as due to the vital selective activity of these cells; if so, the lymph-flow is not directly related to and dependent upon pressure changes in the blood-stream. Pressure changes in the arteries are of small moment in this connection; the essential and important factor is an increased capillary pressure brought about by venous obstruction. In renal disease it is not clear how the venous pressure can be affected to any great extent, whereas the arterial pressure is known to be frequently raised. On physiological grounds there is no evidence to show that increase of arterial blood-pressure will cause any increased transudation of lymph; moreover, in renal disease the occurrence of dropsy and the presence of an increased arterial pressure are not necessarily correlated. It has been supposed that a hydræmic plethora is the direct cause of the dropsy, and some authors regard the scanty urinary secretion as the direct cause of hydræmia and dropsy. It is quite certain, however, that mere suppression of urine will not cause dropsy, clinically or experimentally. Complete calculous suppression, ligature of the ureters, the removal of the kidneys do not cause dropsy. It is the suppression of Bright's disease that is intimately associated with the causation of dropsy, not suppression generally.

It is interesting in relation to this question to note that, although the injection of large quantities of salt solution into the blood-vessels of an animal will not cause general dropsy, even after ligature of the ureters, yet if, previously to this, some vascular area be damaged, as the pleura for instance, by the injection of an irritant, then the hydræmia produced by the injection will cause a most abundant exudation. Further, the injection of considerable quantities of salt solution intravenously after intra-peritoneal ligature of the ureters and free venesection will cause an abundant transudation of fluid, poor in proteid, into the peritoneal cavity. It is asserted, however, that the peritoneal vessels have been damaged by the operative procedures necessary to ligature of the ureters, so that although the blood-state and the transudation produced in this way closely resemble that seen in renal disease, the distribution of the transudation is quite different; seeing that it is characteristic of renal disease to affect the subcutaneous tissues.

The most plausible explanation of the dropsy in certain forms of renal disease is to assume that the capillary walls have been damaged, probably by some material in the blood-stream; and that this, together with the hydræmic plethora, leads to the dropsy. These hypothetical toxic substances cannot, however, be the toxic substances leading to uræmia; as uræmia is so frequently seen, not only without dropsy, but where there has never been dropsy. The form of kidney disease that more especially leads to uræmia is not necessarily associated with the presence of dropsy.

Cohnheim's view, that the dropsy is a kind of subacute inflammation of the skin structures, due to deficient excretory activity of the kidney, is negatived by the composition of the fluid, and by the facts that the dropsy is not limited to the skin, and that complete suppression does not cause dropsy.

It is, perhaps, important, in discussing the pathology of renal dropsy, to recognise the difference between mere hydræmia and hydræmic plethora. In one case the blood is simply poor in solids, the total volume remaining the same; in the other it is not only poor in solids, but the volume of the fluid present is increased. A condition of hydræmic plethora is readily brought about experimentally by the removal of a given quantity of blood, and the immediate transfusion of a much larger quantity of normal saline solution.

Heidenhain's experiments have shown that a number of substances injected into the circulation lead to an increased lymph-flow, apparently by acting on or changing the epithelium of the capillary wall; and this observer considers that substances having this action might be divided into two groups—those the injection of which is followed by the formation of an abundant dilute lymph, and those the injection of which is followed by the formation of a very concentrated lymph; and he considered that he had definite evidence that the lymph is more or less of the nature of a secretion, the composition of which largely depends on the vital secretory activities of the capillary walls. Heidenhain's views have not received uniform support; and many experimenters consider that not sufficient stress was laid by him on the effects produced in his experiments upon the venous pressure. However this may be, the production of an increased lymph-flow, dilute or concentrated, by the presence of abnormal substances in the blood-stream, certainly throws a new light on the mode of production of renal dropsy; but the enigma of its abundance in the subcutaneous vessels still remains, as apparently all authors are agreed that, given a general condition favouring the production of an increased lymph-flow from the blood, the vessels of the peritoneum and of the pleura allow an exudation more readily than those of the subcutaneous tissues. Further, not only do vessels of different regions of the body afford facilities for the production of dropsy, but even when there is a general cause, such as heart disease, the composition of the dropsical fluid is different in different regions; moreover, the fluid in the subcutaneous tissue is always dilute, showing that the permeability of these vessels, at any rate for solids (colloids), is far less than that of the peritoneal and pleural vessels.

[For fuller detail the reader is referred to an article on Dropsy which will appear in a following volume.]

3. Uræmia.—The name uræmia is used for a group of symptoms arising during the course of many renal diseases; always grave, not infrequently fatal, and dependent mainly, but not entirely, upon derangement of the functions of the nervous system. In this way the uræmia of renal disease resembles the acetonæmia of hepatic disease.

Uræmia, more or less severe, may occur in almost all diseases of the kidney; thus it is seen in congestion—active or passive; in nephritis, especially in Bright's disease; in renal cirrhosis; in waxy kidney; in tuberculous, calculous, and cystic diseases; in hydronephrosis, and in consecutive nephritis. Furthermore, patients may sometimes succumb to uræmia with complete suppression, and with but few signs of serious disease of the kidneys. This is sometimes seen after severe injuries to sundry parts of the body, or after operative procedures on the kidney or urinary tract.

Fatal uræmia usually occurs either late in the course of chronic renal disease, or else during the course of acute nephritis very violent and severe in degree. Some of the most remarkable forms of uræmia, however, occur suddenly; either in the midst of apparently robust health, or else when the symptoms of some chronic renal disease have existed for some time, but, owing to their apparently trivial character, have been either overlooked or neglected. The uræmia accompanying fatal calculous suppression, and the uræmia of the granular or cirrhotic kidney, are instances of the latter; the uræmia of scarlatinal nephritis, of chronic Bright's disease, and of waxy kidney are instances of the former.

Uræmia may be classified clinically, according to its mode of onset or according to the nature of the most striking symptoms produced; thus, uræmia may be sudden in its onset and rapid in its course, or it may be gradual in its onset and slow and persistent in its course; the former is characterised as acute, and the latter as chronic. Some cases, however, are very rapid indeed in their progress. It is advisable, therefore, to divide the acute cases into two groups, and thus to recognise three groups in all—the fulminating, the acute and the chronic. If uræmia be divided according to the character of the symptoms produced, two great groups can be recognised: (*a*) the nervous type; (*b*) the gastro-intestinal type. In the former the main symptoms point to disturbance of the nervous system, such as delirium, coma, convulsions; in the latter the principal symptoms point to disturbance of the gastro-intestinal functions, such as nausea, vomiting, and diarrhœa. The gastro-intestinal group corresponds fairly well with the chronic or subacute variety of uræmia; the nervous group with the fulminating and acute varieties. This classification, however, is artificial, since many symptoms in the gastro-intestinal form are probably dependent on the action of poisons on the nervous system. The symptoms in the gastro-intestinal form are remarkably constant: nausea, intense and persistent vomiting, hiccough, and frequently, but not invariably, diarrhœa. After the persistence of these symptoms for days, weeks, or months, according to their severity, certain nervous symptoms ensue; such as cramps in the legs, muscular twitchings, contraction of the pupil, occasional and inconstant delirium, and gradually increasing dyspnœa—possibly of the Cheyne-Stokes variety, but more particularly characterised by its peculiar hissing quality. The delirium gradually gives way to drowsiness and coma, and the patient dies from failure of respiration; sometimes gradually, sometimes with remarkable suddenness.

The symptoms in the fulminating and acute forms are much more protean in their manifestations, and may be divided as follows:—

1. *The eclamptic or epileptiform type.* In this form, with or without previous warning, the patient is seized with an epileptic seizure, usually beginning, like other forms of epileptic seizures, with movements involving the small muscles, then spreading rapidly to the whole body. The fits are frequently repeated, and may be of great severity, the patient passing into a condition allied to the status epilepticus. There is usually unconsciousness, which, however, is not always absolutely complete, and the body temperature falls. The pupils are contracted and the knee-jerks exaggerated; and often—if the fits are very frequent and severe—the body temperature rises considerably, and there may even be hyperpyrexia without the presence of any gross inflammatory lesions in the lungs, or elsewhere, to account for the height of the fever. This type of uræmia in its pure form is not common, except in eclampsia; but epileptiform seizures of a similar type occur in other forms of uræmia.

2. *The maniacal form.*—This, also, is not a common form, but it is seen occasionally in cases of contracted kidney in young adults; sometimes in cases where symptoms of renal disease have existed and been recognised for some time; in other more obscure forms where the onset of violent mental symptoms has been the first indication of the underlying malady. The patient is excited, restless, noisy and sometimes very violent; in two cases under my own observation very distinct cataleptic phenomena were present at intervals. The excitement soon gives way to drowsiness, and then to coma and other distinct uræmic symptoms.

3. *The dyspnœic form.*—Dyspnœa of a peculiar hissing character, as noted by Addison, is common in uræmia; sometimes it is almost the only sign present, even in fatal cases. Such patients are seized with a dyspnœa so intense as in some cases to suggest laryngeal obstruction, the patient sitting up and gasping for breath. The breathing is very noisy, hissing, and asthmatic in type, but there is very frequently no great lividity, and the patient is frequently conscious, and his mind clear. The dyspnœa much resembles the paroxysmal attacks seen in leukæmia; more frequently, however, the dyspnœa is only the accompaniment of other uræmic manifestations, and its peculiar hissing quality in a drowsy patient, with bleeding gums, is very characteristic of the uræmic state. Very violent paroxysms of dyspnœa, so far as I have seen, are most marked in the acute uræmia supervening in cases of contracted kidney. The other or hissing variety is more often seen in chronic uræmia, and greatly resembles the breathing seen after the administration of excessive doses of salicylates. The respiratory rhythm in uræmia is often periodic rather than rhythmic; and the form usually assumed is that known as Cheyne-Stokes breathing. The periodicity affects not only the respiratory rhythm, but other functions also; and in a well-marked case the following phenomena occur—with the waxing and waning of the respira-

tory rhythm the pulse-rate is altered in such a way that the rate is quickened with the noisy breathing, and slows down again during the period of apnœa; the periodic variations in the pulse-rate are not quite synchronous with the periods of respiratory rhythm; there is, so to speak, some slight overlapping; the pupil contracts and dilates, the dilatation occurring with the noisy breathing or just preceding it, and, further, during the period of noisy breathing the patient is restless, subject to irregular muscular movements until during the apnœic period he gives way to complete temporary coma.

These phenomena show that Cheyne-Stokes breathing is something more than a mere periodicity of the rhythm of the respiratory centre, and that many other functions of the nervous system are simultaneously affected. In some cases where Cheyne-Stokes breathing is seen, the patient is not completely unconscious, and a waxing and waning of consciousness may be observed; but this is a rare phenomenon in comparison with the others described above. Cheyne-Stokes breathing is more common in chronic uræmia and in the acute exacerbations of chronic uræmia than in acute and fulminating cases.

4. *The comatose form.*—This is the commonest form of uræmia; and in this form the patient, with or without delirium, passes into a state of drowsiness deepening into coma. Sometimes the coma is preceded by cramps and twitchings, and the latter are usually to be observed, especially in the forearms, during the progress of the case. At other times the coma is preceded by gastro-intestinal phenomena, especially by nausea and vomiting; sometimes by intense headache or amaurosis, partial or complete, and there is always a considerable fall in the body temperature.

Some of the most acute cases of uræmia occur, however, quite suddenly, and without any marked prodromal symptoms; such patients, after a short period of delirium, or even without, suddenly become drowsy and rapidly comatose, with contracted pupils, excessive knee-jerks, and subnormal temperature. During this coma epileptiform fits may occur, but these are by no means an invariable accompaniment of uræmia. In all forms of uræmia the tongue is apt to become dry, brown, and cracked.

Other rarer forms of uræmia may be described, and more especially the following:—

5. *The paralytic form.*—In this remarkable condition a hemiplegia or even a monoplegia may occur suddenly without any gross lesion to account for the paralysis being found after death.

6. A form in which persistent *inability to sleep* is the most marked phenomenon, associated with twitching, cramp and hiccough; but the mind remains clear and there is no coma: death occurs rather suddenly from respiratory failure.

7. *Latent uræmia.*—This is probably the most remarkable of all; it is seen more especially as the result of complete obstructive suppression of urine, and has been fully described by Sir William Roberts. It is seen

when both ureters are obstructed simultaneously; or, more commonly, where bilateral calculous disease has led to the complete destruction of one kidney in the past, and then the ureter of the sole remaining kidney becomes suddenly obstructed, and no urine is passed. Sometimes a very small quantity of urine is pent up in the renal pelvis behind the obstruction, and it is not common in a case of complete suppression to find at the necropsy no urine pent up in this situation. The symptoms in this class are remarkable for their slight intensity, and for this reason the term "latent uræmia" is perhaps applicable to such cases. Such patients will live for seven, ten, or even fourteen days without expelling any urine. They remain conscious almost to the end; and all the so-called uræmic symptoms are conspicuous by their absence. There is but little headache and nausea; vomiting may be absent, and the patient complains of little but weakness and drowsiness. The tongue becomes dry and brown, the pupils contract, and perhaps—after some days of complete suppression—slight twitching of the muscles may be seen. The temperature is subnormal, and this and the state of the pupils are the most frequent and trustworthy signs of a condition, apparently trivial, but really of the utmost gravity. Such patients usually die suddenly from respiratory failure, with little if any mental disturbance or confusion.

Although vomiting is not usually a marked symptom of this condition, cases are sometimes seen where the vomiting is not only well marked, but where it is almost the only symptom present; and in the absence of a complete and accurate history of the case, it may be so severe as to suggest intestinal obstruction: indeed this grave mistake in diagnosis has been made more than once. This symptom group has usually been said to occur in cases of calculous suppression only; but I have seen a precisely similar state where, owing to endarteritis and thrombosis of the interlobular arteries of both kidneys, the renal secretion was practically arrested, and the patient lived for seven days without secreting any urine. The symptoms presented by this patient were those described by Sir William Roberts as characteristic of double calculous suppression.

The difference between the group of symptoms seen in calculous suppression and the ordinary forms of uræmia is very great, and has considerable bearing on the interpretation of uræmia.

Attempts to explain the nervous disturbances in uræmia have hitherto been made on what may be called the mechanical and the chemical bases. According to one school, the results are due to the excitation or paralysis of the nerve structures by the changed physical conditions brought about by cerebral œdema or cerebral anæmia; according to the other, the results are due to the action on the nerve-cells of one or more poisons circulating in the blood-stream.

Cerebral œdema is seen, no doubt, in cases of fatal uræmia unassociated with general dropsy, but the general feeling is that it is rather the result of atrophy of the cerebral convolutions than an active condition. Cerebral œdema was invoked to explain uræmia, as it affords a possibility of accounting for localised uræmic disturbances; modern knowledge, however, certainly shows that a poison circulating in the general blood-stream may pick out but one portion of the nervous system, or even produce a lesion on one side of the body only. Lead and arsenic afford numerous instances of such actions. Both may cause symmetrical peripheral neuritis; but what is more remarkable is that either of them may cause a patch of focal myelitis. Arsenic not infrequently causes herpes, which in all probability is dependent on a nerve lesion, and is generally unilateral in its distribution. Further, one and the same poison may produce opposite effects at different times or in different cases. Thus, lead poisoning may cause convulsions or palsy. The mere fact, then, that uræmic manifestations are sometimes localised, and are not always uniform, does not militate in any way against the view that their source is a toxic one.

An active inflammatory œdema is as familiar to pathologists as a dropsical cerebral œdema is unfamiliar; but there is no evidence of the existence of such a condition in uræmia.

Cerebral anæmia will undoubtedly produce many of the effects so often seen in uræmia. For instance, convulsions, epileptiform fits, Cheyne-Stokes breathing can all be brought about experimentally by ligature of one or more of the cerebral arteries; and it is possible that cerebral anæmia may be responsible for some of the phenomena seen in uræmia. The difficulties in the way of this view are that modern investigation shows no evidence of any well-developed vaso-motor mechanism supplying the cerebral vessels; and further, that the state of the cerebral vessels is mainly dependent on the state of the vessels at large. Contraction of the vessels of the body leads to distension of the cerebral vessels, and cerebral anæmia is more readily brought about by causing dilatation of the vessels of the body than by causing active constriction of the vessels of the brain. In fact, there is no method by which active constriction of the cerebral vessels can be brought about experimentally. It is probable that even if the blood were to contain a substance capable of constricting the cerebral vessels, the vascular constriction and the heightened blood-pressure produced by its simultaneous action on the other vessels of the body would overpower the local cerebral effect.

One of the principal reasons for looking upon uræmia as dependent on physical causes is the fact that uræmia is so often associated with a granular or fibroid kidney. This condition is one in which, owing to the existence of extensive lesions in the vascular system producing great thickening and narrowing of the arteries, it is possible that anæmia of the tissues might be produced.

Uræmia in these cases is common when the blood-pressure is high; and, notwithstanding the thickening in the arteries, the blood-pressure in this disease frequently varies, and a temporary increase in blood-pressure and uræmic manifestations have long been known to be associated. Further, venesection, or a spontaneous hæmorrhage, such as epistaxis, will frequently relieve at the same time both the increased tension and the uræmia. These are the principal reasons that led Traube to form his celebrated hypothesis of cerebral œdema and anæmia. For the reasons mentioned above this hypothesis cannot now be accepted, although there can be no doubt, as just mentioned, that high tension is frequently associated with uræmia. High tension, and even extensive arterial disease, are not necessarily associated with extensive disease of the cerebral vessels; thickening of their walls cannot be inferred by the examination of the pulse, nor by the absence of marked high tension. It is not uncommon to see the cerebral vessels extensively thickened without obvious general disease of the other vessels; and on the other hand, extensive disease of the vessels of the body may exist with comparatively little disease of the cerebral vessels or even none.

For these reasons the majority of observers look upon uræmia as dependent on the presence of toxic material in the blood, and the excitation of the nervous structures by this poison. Unfortunately, however, no such poison has hitherto been separated and identified, and the great variety of uræmic manifestations has suggested the possibility that more than one toxic body is present.

The toxic substance may appear in the blood under one or more of the following conditions: (i.) that a body that ought to be and normally is excreted, is retained; (ii.) the abnormal decomposition in the blood or tissues of such a body; (iii.) the formation of abnormal products of metabolism by the tissues.

The first is the simplest explanation of uræmia, and one very generally accepted. In many cases of subacute and chronic uræmia, and in the violent uræmia seen in acute nephritis, the quantity of urine excreted is often very small, and examination of the blood shows the presence of greatly increased quantities of nitrogenous extractives. The amount of urea in the blood may be twenty times greater than normal; and although this substance may not be directly answerable for the effects produced, its presence in these large amounts serves as an index to the amounts of other and perhaps unknown bodies, possessing toxic actions, which may be present in large quantities. Bouchard has insisted strongly on the fact that the urine normally is toxic, that its toxicity depends on a variety of substances, more especially salts, pigmentary matters, and certain unknown constituents, and that the nitrogenous extractives present in the urine, and more especially the urea, possess but little poisonous action. He conducted a series of observations showing that a certain quantity of urine injected into the circulation is fatal; in some cases death was preceded by convulsions, in others by coma; in nearly all contraction of the pupil and failure of respiration were marked symptoms.

By comparing the amount of urine injected with the weight of the animal, he established what he called urotoxic equivalents, and found, as a mean of a large series of observations, that 25 to 75 c.c. of urine per kilogramme of body weight of the animals used (rabbit) were fatal.

Ligature of the ureters and double complete nephrectomy is usually fatal on the third day, and some of Bouchard's observations tend to show that the amount of urine excreted in three days is toxic if injected at any one time. Bouchard, however, stated that the urine in many cases of uræmia loses its toxicity largely or in part; and he deduced from this that the toxic principles are retained, and produce the well-known symptoms.

The principal difficulties in the way of the acceptance of this view are, in the first place, that when suppression of urine occurs in the human subject, as in cases of calculous anuria, the symptoms produced are as described above, very peculiar, and not those that are usually considered characteristic of uræmia. Secondly, in a very large number of cases of acute uræmia with granular cirrhotic kidney there is often no evidence of any considerable suppression of urine. Such patients often pass very considerable quantities of urine, containing less urea, it is true, than normal, but not necessarily less than many patients, suffering from other diseases and taking but little food, would pass. In my experience it has not been uncommon to find patients dying of acute uræmia with granular kidneys, and excreting as much as 10 to 12 grammes of urea in the last twenty-four hours of life. Moreover, as such patients are usually unconscious, it is impossible to collect all the urine; hence these quantities do not really represent the total amount excreted. Many patients suffering from other diseases with no complication of the kidneys, and even healthy patients, often do not pass more than 10 to 15 grammes of urea per diem. Such may be the case in patients who have undergone ovariotomy and have been kept for twenty-four hours without food.

Patients dying from acute uræmia often take little or no food for many days, and still more frequently reject what they do take; moreover, the urine is often highly albuminous, and the proteid thus excreted represents a nutritive loss; hence it is unreasonable to expect such patients to pass quantities of urea at all comparable to those seen in health, and the mere fact that the excretion may be, comparatively speaking, low, does not prove that the kidney is unable to excrete the nitrogenous extractives.

The blood in cases of ordinary uræmia arising from renal disease contains a large excess of nitrogenous extractives, frequently as much as twenty times the normal. Again, the blood of patients who have granular kidneys, and the blood and dropsical exudations of patients with chronic Bright's disease, contain very considerable quantities of urea and other nitrogenous extractives at a time when the patient is free from obvious uræmic symptoms. The blood normally contains, approximately, 0·015 per cent of urea. In renal disease without uræmia this may rise to 0·15 per cent, and this at a time when the patient is excreting quantities of urea within the limits of health. With the supervention of acute uræmia the quantity may rise in the blood-vessels to 0·4 or even 0·5 per cent.

No experimenter has been able to reproduce all the symptoms of uræmia, either by the injection of urea or of other nitrogenous extractives; and although the blood, in cases of ordinary uræmia, contains this large excess of nitrogenous extractives, such is not the case in eclampsia. Even in fatal cases of eclampsia the blood does not contain quantities at all comparable to those seen either in uræmia or in cases of calculous suppression, the highest percentage observed by myself being 0·06 per cent.

Retention undoubtedly affords the simplest explanation of the presence of these large amounts of extractives in the blood; but I think there can be no doubt that these extractives are present in increased amount at a time when there is no evidence of a greatly diminished nitrogenous output; and further, as mentioned above, the urine contains quite appreciable quantities of extractives, even in the last twenty-four hours of life, since on the whole it is exceptional to see complete suppression of urine in cases of acute uræmia in the granular kidney.

Seeing all these difficulties in the way of explaining uræmia as dependent simply on the retention of some normal constituents of the urine, many observers have fallen back on the view that, owing to the diminished excretory activity of the kidney, the retained urinary constituents undergo decomposition, either in the blood at large or in the alimentary canal. It has been suggested that the urea decomposes into carbonate of ammonia, and that the toxic phenomena of uræmia are due to the presence of this body. Carbonate of ammonia, when injected into the circulation, will undoubtedly produce many symptoms characteristic of uræmia, such as convulsions and dyspnœa. Many observers, however, have failed to detect ammonia in the blood in fatal cases, and for this reason the suggestion has not received any large measure of support. Inasmuch as there are these serious difficulties in the way of the retention and decomposition hypotheses of uræmia, Perls and Schottin suggested long ago that the toxic substances in uræmia might be derived from the products of abnormal metabolism. There are some facts in favour of this view. In the first place, the typical phenomena of uræmia are not those seen as the result of simple suppression. Again, in cases of uræmia, the quantities of nitrogenous extractives in the blood, and more especially in the tissues, such as the muscles, are far greater in percentage amount than in cases of complete calculous anuria. This suggests that the quantities of these bodies are too great to be accounted for by retention.

My experiments, mentioned above, have shown that when the available kidney substance is greatly reduced in amount, the excretory functions of the kidney are not only not seriously interfered with, but that the excretion is actually increased; and that, notwithstanding this, the blood and tissues of the animals contain very large quantities of urea and other nitrogenous extractives. In the experimental cases these nitrogenous extractives must have arisen from increased tissue disintegration, for no retention occurred, but a positive increased excretion of urinary water and urea; and these experiments suggest very strongly that when the available kidney substance is diminished beyond a certain amount—roughly speaking, one quarter of the total kidney weight—the proteid tissues undergo rapid disintegration with the formation of abnormal quantities of extractives. These experiments, then, lend some support to this view of uræmia, although the classical symptoms of uræmia appeared in none of the animals.

4. **Cardio-vascular changes.**—Widespread changes in the cardio-

vascular system are common in renal disease, and more especially in certain forms of it, such as renal cirrhosis and chronic Bright's disease. The pathological changes produced in renal disease involve the heart and the large and small arteries; the former becomes hypertrophied; the changes in the arteries, however, are not so simple. In many cases the large arteries lose their elasticity, but this is by no means a constant change, and in very far advanced renal disease the large arteries may still be very elastic. The inner coat of the larger arteries frequently presents atheromatous changes, but these again are not an invariable accompaniment of renal disease. The medium-sized and small arteries have their coats very much thickened, and this thickening affects mainly the internal coats. In the small arteries the changes are on the whole most evident in the internal coat. The middle coat of the thickened arteries shows an increase in the amount of muscular tissue, and this in some cases is exceedingly well marked. In others, apparently, the increase in this coat is largely dependent on fibroid change; but it is unquestionable that, in many cases of renal disease, there is a true hypertrophy of the muscular coat. The thickening of the internal coat is largely dependent on the formation of loose fibrous tissue in the deeper layers, so that the subendothelial tissue is greatly increased in thickness; this increase is not always uniformly distributed, and not uncommonly the endothelium is thickened also, but this is not so frequent as the thickening in the subendothelial layers. The thickening of the inner coat decreases the lumen of the vessel very considerably, and the thickening of the middle coat—especially when fibroid—is sufficient to be readily recognisable by the finger in such an artery as the radial.

The arterial changes are frequently widespread, but they are not uniformly distributed, and they are most marked in the vessels of the kidney itself: in some cases, perhaps, they are restricted to these vessels.

In addition to the above changes in the arteries miliary aneurysms are commonly present, especially in the cerebral vessels. These miliary aneurysms, it is well known, affect more particularly the small arteries, and they are frequently present in enormous numbers. [*Vide* art. "Disease of Arteries" in a later volume.] The cirrhotic kidney and certain forms of chronic Bright's disease are the renal lesions most frequently associated with the presence of miliary aneurysms, and hence these are the renal diseases in which cerebral hæmorrhage is most prone to occur.

The aneurysms of large vessels, due to atheromatous changes in their walls, are by no means necessarily associated with renal disease; although the high arterial tension existing in renal disease is usually held to be one of the remoter causes of aneurysm.

Hyaline changes in the capillaries, especially in those of the glomeruli, are commonly associated with the cardio-vascular changes described above.

The cardiac hypertrophy of renal disease is usually moderate in amount, and unless there be coexisting valvular defects it does not attain the degree which is seen in the latter condition. The hypertrophy of renal disease affects the left side of the heart mainly yet not exclusively; but unquestionably the hypertrophy of valvular disease affects the right side of the heart more than the hypertrophy of renal disease does. Still in the latter case, if the enlargement of the heart be considerable, the right side shares in it to a slight extent.

These widespread lesions of the vascular system are most extensive in certain cases of renal cirrhosis; more especially in that condition known as red granular kidney, or raspberry kidney, which occurs in middle-aged persons; and the greater and more widespread the arterial disease the greater the cardiac hypertrophy. The vascular lesions are also fairly well marked in cases of chronic Bright's disease, where the size of the kidney may be variable, sometimes a little larger than the normal, sometimes a little smaller, but where there is considerable fibroid change in the kidney. These cases often occur in the comparatively young, and the arterial thickening and cardiac hypertrophy may occasionally in these cases reach the degree seen in the granular kidney. Such patients may succumb to cerebral hæmorrhage. On the other hand, cases of chronic Bright's disease with the kidneys shrunken and fibroid, the capsule thickened and leaving a granular surface on stripping, may exist with comparatively little hypertrophy or arterial change except in the renal vessels. It is not very uncommon to see cases of death from uræmia with the kidneys weighing about three ounces apiece, and very granular on the surface; but the stripping of the capsule does not tear the cortical substance, and in such cases the heart may not be appreciably enlarged, and the arteries generally are not thickened to any great extent.

The amyloid kidney is not associated with any profound arterial changes except those necessarily associated with the presence of waxy disease in the body; and the heart in these cases is not hypertrophied.

Extensive destruction of the kidney substance by hydronephrosis, even if double, is not necessarily associated with profound cardio-vascular changes. On the other hand, in some cases, and more especially perhaps in the double hydronephrosis seen in young persons and probably dependent on congenital abnormalities, the cardiac hypertrophy is a well-marked phenomenon. Cases of partial hydronephrosis associated with fibroid change in the rest of the kidney are not uncommonly seen; the upper or anterior half of the kidney is little more than a sac, and the available kidney substance is spread out in the posterior or lower portion. In such cases cardiac hypertrophy is often a marked feature.

Acute and subacute Bright's disease lead very rapidly to the production of high arterial blood-pressure, and cardiac hypertrophy and arterial changes, if the malady last so long as six weeks, may be observed; that is to say, in this time obvious physical signs pointing to the existence of hypertrophy can be detected. Many cases of chronic Bright's disease associated with dropsy exist for long periods without leading to the marked cardio-vascular changes associated with high pressure.

From the above facts the following deductions may, perhaps, be possible. High arterial blood-pressure is a frequent accompaniment of renal disease, and more especially of the condition known as the granular kidney occurring in middle-aged persons. It is also well marked in the contracted kidney occurring in the young, as a sequel to acute or chronic nephritis; but it is not an invariable accompaniment of these conditions. Finally, extensive destruction of both kidneys may take place without necessarily producing the graver widespread vascular lesions associated with high blood-pressure.

The explanation of the cardio-vascular changes accompanying renal disease, and especially evident in certain forms of it, is by no means simple. It is usually supposed that a condition of what has been called "functional high tension" precedes the anatomical changes described above; that is to say, the blood-pressure is increased as a result of an increased activity of the vaso-motor system with consequent contraction of the arteries; the excitation of the vaso-motor mechanism being produced by the circulation in the blood of some material capable of exciting it. In favour of this opinion is the undoubted fact that the pulse in renal disease frequently shows the characteristic features of high pressure, when there may be no clinical evidence of anatomical changes in the vessel. This is more especially true of acute renal disease. Further, the degree of pressure is variable, and a smart hæmorrhage, say, from the nose, will often relieve it greatly. There is, however, no evidence to identify the substance or substances that cause this functional increased activity of the vaso-motor system, and some authors have supposed that the cardiac hypertrophy is not the result of the vascular obstruction, but actually the cause of it; and they consider that the circulation in the blood of increased amounts of nitrogenous metabolites, such as urea and its allies, causes an increase in the force of the heart-beat, and that in this manner the vessels are exposed to an increased strain, the results of which are the thickening and other changes observed in the arteries.

At any rate, the injection of urea temporarily increases the blood-pressure, yet this substance has certainly no influence in causing arterial constriction; if therefore the high tension of renal disease depends on the presence of increased amounts of nitrogenous extractives in the blood, the effects may be produced by a primary action on the heart.

Again, it has been suggested that the high tension of renal disease is brought about by an attempt to maintain an efficient rate of blood-flow through the remaining kidney substance; now inasmuch as this area is greatly diminished in extent, the flow can only be maintained at a normal rate by an increase in the general blood-pressure produced by constriction of other vascular areas causing an increased rate of flow through the remains of the kidney.

Speaking broadly, the high pressure in renal disease certainly varies inversely as the extent of kidney substance present; and it reaches its maximum in renal cirrhosis. Experimentally, I was unable to reproduce the characteristic lesions seen in the arterial degeneration of renal disease as the result of the removal of large quantities of kidney, but the blood-pressure was apparently raised.

In many cases of renal cirrhosis it is probable that the widespread arterial changes are primary, and that the lesions in the kidney, especially those in the epithelium, are secondary to the vascular lesion; in other words, the interference with the circulation through the kidney leads to the decay of the higher renal elements, and thus the overgrowth of fibrous tissue subsequently found in the kidney is secondary to this, and not a primary lesion. [*Vide* art. "Arteriosclerosis" in a following volume.]

Considerable lesions of the smaller vessels of the kidney, with great thickening of their walls and a narrowing of their lumen, may, however, exist without the presence of any cirrhosis.

Albuminuric retinitis and thickening and rigidity of the retinal vessels are common accompaniments of grave renal disease; more especially in the later stages of chronic Bright's disease and in the granular kidney.

5. Marasmus and Anæmia.—Renal disease frequently produces well-marked anæmia, and also great wasting. The extent of the latter may be very largely concealed by the presence of dropsy. In some renal diseases emaciation is one of the early symptoms. The wasting of renal diseases is dependent on many causes. In the first place, such patients have an impaired nutrition, dependent on serious disorders of the gastro-intestinal tract: the appetite is poor; nausea, vomiting, and diarrhœa are common. The quantities of albumin lost in the urine are often considerable, especially in chronic Bright's disease; and in this way the nutrition of the patient is still further affected, since such patients frequently pass in the urine one-quarter or one-third of the total proteid ingested. Wasting, however, may be a marked feature of renal cirrhosis, in which the disturbance of the gastro-intestinal functions may be slight, and in which the albuminuria is always slight; the emaciation in these cases resembles the rapid wasting that is seen experimentally when large quantities of the kidney substance are removed, a condition which I have shown—at any rate experimentally—to be dependent on an increased disintegration of the proteid tissues, more especially of the muscles.

Anæmia in renal disease is present in almost all cases to a greater or less extent; but it is specially marked in chronic Bright's disease associated with dropsy. Such patients are exceedingly pale. Many patients with granular kidney, especially in the form of it seen in young persons, are also frequently very pale; and the anæmia of renal disease, like the wasting, is often of complex origin. Many patients suffer from profuse hæmorrhages, specially from the nose or from the urinary tract; and in the latter case, if very profuse, it not improbably arises from the pelvis of the kidney. The dyspepsia and gastritis necessarily present in this disease will also tend to cause anæmia, and it is probable that the widespread disorders of nutrition also tend in this direction.

The anæmia of renal disease may be so severe as to approximate in character to the anæmia of pernicious anæmia; and many of the vascular murmurs characteristic of anæmia are very evident in cases of renal disease.

6. Secondary Inflammations.—Inflammatory complications are common in certain forms of renal disease, and more especially in chronic

Bright's disease associated with dropsy. Such patients often suffer from septic inflammations of the skin and subcutaneous tissues after incisions have been made for the relief of dropsy; and it is well known that formidable septic complications are much more apt to ensue after incisions in the treatment of renal than in that of cardiac dropsy.

Deep-seated inflammations of organs and of serous membranes are also very frequent; and low forms of pneumonia are common in uræmia complicating any form of renal disease. Pericarditis is also a very common complication of renal disease, and it is remarkable that it frequently assumes a latent form; other inflammatory complications, such as pleurisy and peritonitis, are also not uncommon.

It was at one time supposed that these inflammatory complications are directly dependent on the presence in the blood of the toxic substances causing uræmia. Modern knowledge has shown, however, that these inflammations have a microbic origin, and that in renal disease the resistance of the tissues to microbic infection is seriously diminished. As mentioned above, in the section on "Urine," micro-organisms are not uncommonly present in the urine of Bright's disease; it is probable, therefore, that these organisms are circulating in the blood: if this be the case, it is comparatively easy to understand the frequency of grave inflammatory complications in this disease. Not only are inflammatory complications common in renal disease, but they rarely run a normal course: thus inflammations of the serous cavities have a great tendency to become purulent, and this is especially the case in pericarditis.

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REFERENCES

1. ABRAM, J. H. "Acetonuria," *Journal of Pathology*, vol. iii.—2. BOUCHARD, CH. *Les auto-intoxications*, 1887.—3. BRADFORD, J. R. "Influence of the Kidney on Metabolism," *Proc. Roy. Soc.* 1892.—4. CHARCOT. *Traité de médecine*, vol. v.—5. DUNLOP. "Oxalic acid in Urine and Oxaluria," *Journal of Pathology*, vol. iii.—6. EBSTEIN. *Die Natur und Behandlung der Gicht*. 1882.—7. GARROD, A. "The Yellow Colouring Matter of the Urine," *Proc. Roy. Soc.* vol. lv.—8. GARROD and HOPKINS. "The Occurrence of Hæmatoporphyrin in the Urine of Patients taking Sulphonal," *Journal of Pathology*, vol. iii.—9. HOPKINS. "On the Estimation of Uric Acid in the Urine," *Journal of Pathology*, vol. i.; see also FOKKER, *Pflüger's Archiv*, Bd. x.; and SALKOWSKI, *Virchow's Archiv*, Bd. lxviii.—10. LEATHES and STARLING. "Production of Pleural Effusion," *Journal of Pathology*, vol. iv.—11. LUFF. Goulstonian Lectures, R.C.P. London, 1897.—12. MACMUNN. *Clinical Chemistry of the Urine*, 1889.—13. MCWILLIAM. "New Test for Albumin and other Proteids," *Brit. Med. Journ.* 1891.—14. ROBERTS. *Uric Acid, Gravel, and Gout*, 1892.—15. SALKOWSKI and LEUBE. *Die Lehre vom Harn*.—16. VON JAKSCH. *Clinical Diagnosis*.

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CIRRHOSIS OF THE LIVER

General considerations. — The term "cirrhosis" comprises a group of diseases of the liver which, though they differ widely in their causation and clinical importance, have this feature in common, that the organ becomes permeated to a greater or less extent by a newly-developed fibrous tissue. The word "cirrhosis," which, from the tawny yellow colour assumed by the hepatic tissue, was originally given to a common form of the disease (Laennec), is now in general use to denote any fibroid change in the liver; and it is not infrequently applied to a similar morbid change in other organs.

This newly-developed fibrous tissue in the liver is distributed in various ways, and a classification of the different forms of cirrhosis might be based upon its arrangement and distribution, though it is not to be supposed that such anatomical varieties are absolutely distinct. In the most common variety of the disease it forms a coarse network which permeates the whole organ, and encloses in each mesh a number of the hepatic lobules (multilobular). In a less common variety a finer network of new fibrous tissue tends to surround individual lobules (unilobular); and in this form a plexus of bile-ducts, apparently newly formed, is often present around the lobules. In another form the new tissue is found to penetrate the lobules themselves, often surrounding and isolating individual cells or groups of cells (intralobular or pericellular). In a fourth variety, which is usually considered under the head of cirrhosis, dense bands of cicatricial tissue traverse the whole or a large part of the liver, cutting it up into irregular masses, and producing by their contraction considerable deformity of the surface of the organ (gummatous or syphilitic cirrhosis).

Classification.—To classify the various forms of cirrhosis according to these anatomical characters is not, however, clinically useful, inasmuch as the points of distinction between them are seldom recognisable during life. On the other hand, a classification based on the causation and mode of origin of the disease cannot, in the imperfection of our present knowledge, be thoroughly carried out. But, notwithstanding its scientific imperfection, such a scheme is practically useful; and it will be adopted here so far as our knowledge permits, as follows:—(A.) Alcoholic cirrhosis, (*a*) Multilobular form; (*b*) Unilobular form, to which is appended an account of the form commonly known as "biliary cirrhosis." (B.) Malarial cirrhosis. (C.) Syphilitic cirrhosis. And mention will be made of certain minor forms of cirrhosis which are rather of pathological than of clinical interest.

Etiology.—The excessive use of alcohol is by far the most common cause of cirrhosis of the liver in all countries; by its side all the other causes together are insignificant. As regards the form of alcohol, statistics show that spirits of some kind are in most cases answerable for the disease; but it is certain that the more dilute forms of alcohol, beer and wine, are capable of producing a like result.

The amount of alcohol which is necessary to produce the disease is found to vary greatly. When a patient first comes under observation with the signs of cirrhosis, there may be a history of many years of slight daily alcoholic excess, to which the name of intemperance is given only after the appearance of symptoms of alcoholic poisoning; or he may be an habitual drunkard; or there may have been a short period of indulgence, not amounting to more than a few months, in a person previously temperate. The degree of cirrhosis has no constant relation to the total amount of alcohol taken. A history of great habitual alcoholic excess may sometimes be obtained from patients who present no evidence of cirrhosis. It is possible that this variation in the result may depend on such factors as the degree of dilution of the alcohol, or the relation of its ingestion to the taking of food; moreover, it is not improbable that individuals differ greatly in their susceptibility to the poison.

The disease, as produced by alcohol, is chiefly met with in males, in whom it is three or four times as common as in females. It occurs at almost any age. Cases, undoubtedly due to alcohol, have been recorded as occurring at the extreme ages of six and ninety, but the chief incidence of the disease, as might be expected, is in middle and late life, and statistics show that in about two-thirds of fatal cases death occurs between the ages of thirty-five and fifty.

As will be subsequently described, two forms of cirrhosis—the multilobular and the unilobular—must be recognised as due to alcohol. At present our knowledge is not sufficient to determine whether this anatomical difference depends on the form of the alcohol, or on the mode of taking it, or on some other factor. There is, however, some evidence to connect a large and highly fatty variety of multilobular cirrhosis (sometimes called fatty cirrhosis) rather with beer than with other kinds of stimulant.

Syphilis, both hereditary and acquired, stands next to alcohol in importance as a cause of cirrhosis. The form of disease commonly produced by hereditary syphilis is truly a cirrhosis or general fibroid condition of the organ. The results of acquired syphilis must also be considered under this head, although it leads rather to a localised fibroid change or scarring of the liver, to which the name cirrhosis is not so strictly applicable.

Further, it may be accepted that a cirrhotic condition of the liver may supervene as the direct result of chronic malarial poisoning (Kelsch and Kiener). The cirrhosis may be looked upon as a sequel of the chronic congestion of the liver which is apt to ensue in patients who have been the subject of repeated attacks of intermittent fever; but in some instances the possibility of the association of alcoholic excess must be borne in mind.

Certain minor forms of cirrhosis occur under other conditions; but in such cases the change rarely reaches such a degree as to produce recognisable symptoms. Thus a deposit of tubercles in the liver may be accompanied by a definite though slight degree of hyperplasia of the *interstitial tissue in the portal canals; and this event is most common in association with a chronic tuberculous peritonitis* (Hanot and Gilbert). The common enlargement of the liver in rickets has been occasionally found associated with a similar slight increase in the portal connective tissue. Finally, a cirrhosis, sometimes of a high degree, may result from the absence or atresia of the common bile-duct, which is occasionally met with in new-born infants (*vide* p. 253). Life, in such cases, is seldom prolonged beyond a few months, and death occurs from the jaundice rather than from the cirrhosis; yet the latter may be sufficient to give rise to ascites.

In conclusion, it may be safely stated that in nearly all patients who present definite signs of cirrhosis the disease has arisen as a consequence of alcoholic excess, syphilis, or chronic malarial infection.

Still, when these three causes have been duly considered, a certain small proportion of cases of cirrhosis will remain in which there is room to doubt whether any one of the three has been in operation. It must be remembered herein that it is not always easy to elicit a history of alcoholic excess—there being sometimes a purposeful, and more often an unconscious tendency on the part of the adult patient to reticence in this matter. In the case of young children it may be found that spirits or beer have been administered to them occasionally by their parents, but it may be impossible to ascertain exactly to what extent this practice has been pursued It has been suggested that cases of cirrhosis, in which there is no history of alcoholic excess, may be the outcome of a previous fever, such as scarlet fever, measles, typhoid fever, or pneumonia; inasmuch as in many specific fevers slight inflammatory changes in the portal tissue may be found after death (Botkin, Klein, Welch). The connection of such changes with a later development of definite cirrhosis is not proved, but it is at any rate probable that some factor in the causation of this disease is still missing.

It is frequently stated that long-standing obstruction of the hepatic or common bile-ducts may result in the development of cirrhosis. It has, indeed, been repeatedly shown that ligature of the common duct is followed in some lower animals by a remarkably rapid development of a cirrhosis of unilobular distribution (W. Legg, Charcot and Gombault). It is true that a slight hyperplasia of the portal connective tissue may certainly be observed with the microscope in some instances of obstructive jaundice in man, especially when the obstruction has been due to carcinoma in the head of the pancreas.[1] There may be increased cellularity of this tissue, and there is sometimes evidence of an acute and, it may be, of a suppurative inflammation in it. And as has been already mentioned, congenital absence or atresia of the common duct in children may undoubtedly be associated with a high degree of cirrhosis. Yet notwithstanding this positive evidence, it is established by the overwhelming negative testimony of the post-mortem room that biliary obstruction in man does not result in any degree of cirrhosis sufficient to produce symptoms. The discrepancy between experimental and clinical evidence on this point may be explained by the difference *in the condition which causes the biliary obstruction in the two cases. There is no event* in man which is comparable to the drawing of a ligature round the outside of the common duct and its sheath of connective tissue.

Finally, a cirrhosis has been described as accompanying the congestion of the liver which results from chronic cardiac and pulmonary disease. The liver, in this condition, is often finely granular on section, owing to the sinking of the centre of the lobule below the general level of the cut surface. But though there is sometimes a slight hyperplasia of the connective tissue in the centre of the lobule, nothing worthy to be called cirrhosis is produced in this way.

A. ALCOHOLIC CIRRHOSIS.—It is now generally recognised that two forms of cirrhosis of the liver are induced by the excessive use of alcohol. These two forms are separated by differences both in their morbid anatomy and in their clinical features, and they must be separately considered.

In the first form (*a*), which is by far the most common, the newly-developed fibrous tissue tends to surround large groups of hepatic lobules, and it is therefore spoken of as "multilobular." This form is commonly associated with ascites, but seldom with jaundice. In the second and less common variety of alcoholic cirrhosis (*b*), the new tissue is developed for the most part around single lobules, and it is consequently described as "unilobular." In the latter case there is but little tendency to ascites, while jaundice is a common event. In this unilobular form a number of bile-ducts, apparently new formed, are generally found in the interlobular connective tissue. This appearance gave origin to the hypothesis of a cirrhosis starting around the small bile-ducts—a "biliary cirrhosis"—and the question of such an origin in some cases will be presently considered.

The terms "atrophic" and "hypertrophic," as applied to the multilobular and unilobular forms respectively, are scarcely worth retaining. The term atrophic has lost much of its fitness, now that statistics show that the hobnailed liver, to which it was originally applied, is not necessarily small, but is often increased both in size and weight. And the phrase hypertrophic cirrhosis has become so complicated by the postulate of a biliary cirrhosis that its significance is vague and uncertain.

(*a*) **The multilobular form.**—(*Synonyms* · Laennec's cirrhosis, hobnailed liver)—,

Morbid anatomy.—This variety includes the great majority of the cases of cirrhosis met with in practice.

The liver, as found in a fatal case, is often reduced in size, but this reduction is not invariable, as was at one time supposed. In many instances it retains its normal dimensions, and sometimes it is moderately enlarged, so that its free edge may be felt during life. When thus enlarged, it is generally found that the hepatic tissue is in a highly fatty condition. It is often stated that the liver in this form of cirrhosis is commonly enlarged at the outset of the illness, and that it becomes reduced in size during its course. Though this progressive reduction in size is intelligible on general pathological grounds, and, indeed, clear instances of it (mostly in children) have been recorded, yet there is no evidence to show that such a change is of frequent occurrence. It is possible that the liver may be enlarged in the early stage of the illness, during which the symptoms are so slight that the patient does not come under medical observation; but if a patient be seen with the recognised symptoms of cirrhosis, and the liver be large enough to be felt in the abdomen, it is exceptional at any rate for any diminution in its size to be observed at a subsequent period.

The weight of the hepatic tissue is increased by the cirrhotic process, thus, though the liver is often diminished in bulk, its weight is seldom below that of the healthy organ (50 to 60 oz. in the adult). Its weight may, however, fall to 30 oz. or even less; on the other hand, it may rise to 80, especially if its tissue be fatty. A series of 100 consecutive cases in adults taken from the records of St. Thomas's Hospital shows a minimum of 32 oz., a maximum of 74 oz., and an average of 52 oz.

Owing to the contraction of the new fibrous tissue there is commonly some alteration in the shape of the liver, especially when there is much diminution in size. Its sharp edge becomes blunter, or the whole organ may tend to become globular; the left lobe is often more affected than the right, and may be reduced to a small triangular appendage.

The peritoneal covering is usually much thickened, and is often fixed to the diaphragm, and perhaps to adjacent organs, by close adhesions or tough fibrous bands. There may be evidence also of the extension of this chronic inflammatory process over the whole or a large part of the peritoneum, which may be found whitened, thickened, and opaque.

Whether the liver be of normal size, or small, or enlarged, both the natural and the cut surfaces of the organ in this form of cirrhosis are either covered with minute granulations, or studded with nodules varying in size from a pin's head to a pea. The cut surface especially presents the appearance of rounded islets of yellow or yellowish-brown hepatic substance surrounded by gray or grayish-red bands of fibrous tissue, both of which elements can be easily recognised with the naked eye. The substance of the organ is always exceedingly tough and hard, and the induration is greater than in any other form of cirrhosis.

Owing to the compression exercised upon the portal branches by the new fibrous tissue, there is considerable obstruction to the flow of blood in the portal vein. In rare cases the stagnation is such that thrombosis has occurred in its main trunk and branches. A far more common manifestation of this portal obstruction is the dilatation of some or all of the vessels, which form the points of communication between the portal and the general venous systems. This compensatory dilatation will be subsequently described.

Microscopical examination of a liver in an early stage of cirrhosis shows clear evidence of inflammatory change in the tracts of connective tissue which support the ramification of the portal vein throughout the whole organ. These so-called portal canals are seen to be packed with leucocytes and connective tissue cells in a state of active proliferation. Here and there columns of such fibrifying tissue may be seen advancing between the hepatic lobules; and by the junction of such columns a wide-meshed network of developing fibrous tissue comes into being throughout the whole organ. In the late stage in which the examination is commonly made, this network is seen to consist of dense fibrous tissue which may be still richly nucleated in parts, but has generally lost the highly cellular character seen at an earlier period. At the same time the main portal branches, which at an early stage are often widely dilated, become narrowed and compressed by the contraction of the new tissue in which they run. This new tissue, however, is by no means anæmic; for it can be shown, by injection from the hepatic artery, that it is richly supplied with capillaries in connection with that vessel; and it is probably due to this accessory blood-supply that the functions of the liver are so little interfered with. In some cases there is an apparent development of a few new bile-ducts in the strands of the fibrous tissue. The origin of these will be considered in connection with the second or unilobular variety of cirrhosis, in which they form a more frequent and conspicuous feature.

The nodules of hepatic tissue, which are contained in the meshes of this fibrous tissue, consist of many lobules compressed together. But owing to this compression the lobular arrangement is obscured, and it is difficult to say how many lobules each node comprises. Here and there also a single lobule or a single group of pigmented hepatic cells may often be seen as an islet in a broad fibrous strand.

In advanced cirrhosis the liver-cells are invariably degenerate; they are finely granular or filled with coarse pigment granules, and their nuclei do not readily stain. They are also often filled with large fat globules, and this is especially found to be the case when the liver is of normal or of increased size.

As regards the interpretation of these morbid changes, it may be taken as certain that they are produced by the action of alcohol entering the liver by the portal vein. But these morbid changes are twofold. There is both a degeneration of the hepatic cells and a development of new fibrous tissue; and it is by no means certain whether either of these changes is dependent on the other, or whether both changes are concomitant effects of the alcoholic poison. It has been argued that the hyperplasia of the connective tissue is consecutive to a primary degeneration of the hepatic cells and dependent upon it; that it is such a hyperplasia, in fact, as is known to occur around degenerate and diseased structures in all parts of the body. And in favour of this view, that the cell-degeneration is the exciting cause and not the effect of the fibrous overgrowth, it is pointed out that, although there is undoubtedly a high degree of pressure exerted upon the liver-cells, yet, inasmuch as the development of new vessels from the hepatic artery takes place step by step with the growth of the new fibrous tissue, the blood-supply is still ample, and there is not that mechanical anæmia present which would be likely to cause such an extreme cellular degeneration. On the other hand, if specimens of early cirrhosis are examined from cases in which death has occurred from some other cause, no doubt can be entertained that the interstitial change is essentially an inflammatory one, and that it has its starting-point around the main branches of the portal vein at a time when the appearance of degeneration of the hepatic tissue proper is either scanty or absent.

Consequently, though it is possible that the cell-degeneration may in part be a primary change, and the direct result of the action of alcohol upon the cell, and though it is possible that this cell-degeneration may play some part in the production of symptoms, yet it is quite out of proportion to the vast overgrowth of fibrous tissue. The balance of evidence is strongly in favour of the fibrous overgrowth being a primary morbid change, and it is certainly responsible for the chief symptoms of the disease.

Symptoms.—It can be readily understood, from what has been said as to the morbid process in the liver, that the symptoms attending the early stage of cirrhosis are usually slight and equivocal. The more severe and distinctive symptoms do not appear until the new fibrous tissue has begun to compress the branches of the portal vein

In this early stage the patient is liable to dyspepsia with nausea or vomiting, especially in the morning. The appetite fails, being often better in the later than in the earlier half of the day; the tongue becomes furred; there is a sensation of heaviness or distension after meals, and gaseous eructations are of frequent occurrence. The bowels become irregular, at one time costive, at another time loose, there is often a tendency to hæmorrhoids; and perhaps slight yellowness of the conjunctivæ may be noticed from time to time. Such symptoms may, of course, be merely the direct effect of alcoholic excess upon the stomach and intestinal canal; but their occurrence and persistence in a person who has been addicted to alcohol for some considerable time are sufficient to suggest the presence of cirrhosis in an early stage. This suspicion would be strongly confirmed if at the same time some palpable enlargement of the liver should be detected.

As the morbid process in the liver continues, the obstruction to the portal circulation increases in degree. A very definite train of signs and symptoms ensues, some of which are the direct result of the portal obstruction, while others are the consequence of the impairment of the hepatic function. It is in this stage that the disease is commonly recognised for the first time.

One of the direct results of the portal obstruction is the appearance of ascites. It is not invariably present, but it occurs in at least 80 per cent. The portal system is not completely isolated, but has communication at many points with the general venous system, and by the opening up of these channels of communication, in the manner that will be described, so much relief may be afforded to the obstructed portal system that in some few cases little or no ascites may arise.

The ascitic fluid is clear, straw-coloured, and alkaline, with a specific gravity varying between 1010 and 1015; it contains from 0·4 to 2·0 per cent of proteid, and it either has no power of coagulation or it deposits a very light clot very slowly. If there be any coexistent peritonitis, as is often the case, the percentage of proteid and the power of spontaneous coagulation are thereby proportionately increased. A trace of sugar is occasionally found in it. The amount of fluid varies greatly, but if it be not removed by paracentesis it may reach the enormous quantity of four or five gallons. It may accumulate so slowly that many months may elapse, after its first recognition, before paracentesis becomes necessary; or it may accumulate so rapidly that as much as thirty-four pints of fluid may be removed within five weeks of a previous tapping by which the abdomen had been emptied as far as possible. The relation between hepatitis, peritonitis, and hepatic cirrhosis in the causation of ascites in these cases is not yet fully understood. Dr. Hale White (*vide* art. "Perihepatitis") is of opinion that the ascites proper to cirrhosis is a late event for which more than one tapping is rarely required; and that in the cases of ascites which admit of many tappings, the effusion is due rather to peritonitis.

Another result of the portal obstruction is the state of passive hyperæmia in which the stomach and intestines are maintained, upon this there follows a very constant and persistent catarrhal condition of the mucous membrane. Digestion is imperfect, gastric fermentation and flatulence are common, and there is often a marked tendency to nausea or vomiting in the morning, which is probably attributable to the mucus accumulated in the stomach during the night. The action of the bowels is also irregular; the motions are often pale and unformed, and diarrhœa is at times profuse and uncontrollable.

Further evidence of portal obstruction may be obtained from the direct and indirect results of the opening up of the anastomoses between the portal and the general venous system.

The vessels by which anastomosis is effected become dilated and even varicose, and the results are of considerable importance. There are three important points where this effect is produced.

(i.) The plexus of veins at the cardiac end of the stomach communicates with a similar plexus in the lower end of the œsophagus, the vessels of which open into the azygos veins. Consequently in many cases of cirrhosis there is extreme dilatation of the veins in the lower three or four inches of the œsophagus; and longitudinal submucous vessels, up to a quarter of an inch in diameter, may be readily demonstrated there by means of injection or inflation with air.

(ii.) One or more small veins (parumbilical) constantly run from the left division of the portal vein in the round ligament alongside of the obliterated umbilical vein to the umbilicus, where they communicate with the epigastric system. It is common, as a result of the portal obstruction, to find a large vein developed here, which often reaches the size of a crow-quill. A much larger size has indeed been recorded.

(iii.) Finally, there is a variable degree of communication between *the inferior mesenteric and hæmorrhoidal veins.*

Other less important communications exist by which some of the blood may be diverted. There are the minor accessory portal veins of Sappey, which lie in the areolar tissue and peritoneal folds around the liver, and communicate on the one hand with the portal system, and on the other with the phrenic veins. In some cases enlarged vessels are visible after death on the under surface of the diaphragm, and this means of relief to the portal system may be aided when the liver is firmly adherent to the diaphragm. There is, moreover, some slight communication between the veins of the pancreas, duodenum, colon and rectum, and the retro-peritoneal veins.

A direct consequence of the passage of blood from the portal vein, by the parumbilical vein, to the epigastric system is the occasional appearance of a network of dilated superficial veins around the umbilicus More commonly a few large vessels are seen running from the neighbourhood of the umbilicus downwards to the inguinal regions, upwards to the costal margin, and perhaps extending to the lower part of the thorax The subsidence of ascites is sometimes coincident with the appearance of these vessels. In connection with the dilatation of this parumbilical vein, it may be mentioned that a continuous venous murmur may occasionally be heard with the stethoscope immediately below the ensiform cartilage. The sinuous line of small distended venules, which is often seen round the lower ribs along the line of attachment of the diaphragm, may be equally present in health, it has no special significance in this connection. The formation of hæmorrhoids, again, is a common phenomenon resulting from the communication between the engorged portal system and the hæmorrhoidal veins; but it is too common a malady to be of great diagnostic importance.

Indirectly related to the portal obstruction is the common occurrence of hæmatemesis, or melæna, or both. It is possible that a general oozing from the congested capillaries of the stomach may be the source of the smaller quantities of altered blood which are sometimes vomited; but it is probable that the larger hæmorrhages are due to ulceration or rupture of one of the varicose veins already described as lying in the walls of the cardiac end of the stomach, and more especially in the lower end of the œsophagus. In the former situation punched-out ulcers have been found communicating with a vein, but the latter is probably by far the most frequent site of profuse hæmorrhage. The hæmorrhage may be very profuse and may be quickly fatal, as may be understood from the size of these œsophageal varices. More than four pints of venous blood may be lost in this way, and the bleeding may recur at intervals of a day or two until death results. In most cases, however, the hæmatemesis, though fairly profuse, is not so alarming; and, as it is usually the first grave symptom, many months or even years may elapse before death occurs. Melæna has been known to result from an ulcer in the bowel, but in most cases the hæmorrhage either springs from the stomach, whence the blood *is passed on into the bowel, or from the rupture of distended capillaries in the intestinal mucous membrane.*

It will be understood, from the origin of these dilated anastomotic veins, that they form a compensatory mechanism for the relief of the overcharged portal system; and, consequently, it may be surmised that when they are much developed and are likely to give rise to severe hæmorrhage, there is not much tendency to ascites. Clinical evidence agrees with this anticipation, and profuse hæmorrhage is actually not common in cases of considerable ascites; on the other hand, a sudden hæmorrhage has proved fatal in cases where ascites is absent.

The spleen, which is nearly always found in the post-mortem room to be enlarged and indurated, and commonly weighs from 10 to 15 oz., may sometimes be felt during life; but in most cases it is obscured by the presence of ascites Occasionally it escapes all change, even when the portal obstruction has been severe, and this is probably attributable to its extensile structure.

The liver may often be felt below the ribs, and its edge may project downwards for one or two inches, so that its hardness, and possibly its nodular character, may be recognised. More commonly, however, it is masked by the ascites; though even then it may often be felt by a sudden dipping movement of the hand, which displaces the overlying fluid. The recognition of a small liver is a matter of greater difficulty; and generally speaking, considering the frequent flatulent distension of the bowels, not much stress can be laid on a resonant note at the right costal margin. Attacks of pain over the liver, and more frequently over the spleen, may occur from time to time; and these are doubtless to be attributed to attacks of local peritonitis [*vide* art on "Perihepatitis," page 118]. Tympanites is often a troublesome symptom, which may materially add to the gravity of a case by the production of collapse of the basal parts of the lungs.

Jaundice is ordinarily absent throughout the entire illness; there is nothing more than a yellowness of the conjunctivæ, and a sallow, icteroid complexion. If present it is usually slight, and it may subside and disappear. The urine is often diminished in amount, and presents abundance of urates and sometimes bile pigment. If albumin be present, it is generally due to coincident disease of the kidneys. Even at an early period the feet and shins may become slightly œdematous, but the œdema is not marked unless the ascites be so considerable as to aid in its production by pressure on the inferior vena cava. Œdema of the abdominal wall may also be noticed occasionally, and is presumably due to that disturbance of the venous circulation in it which has been already described. Often in a late stage there may be effusion of fluid into one or both pleuræ; this may be of simple origin, but often it is found to be due to a tuberculous pleurisy. As a rule there is no fever in this form of cirrhosis; but if a patient be under continual observation for a long period, we may often observe an occasional rise of two or three degrees for a few successive evenings.

The distended capillaries on the cheeks, the so-called "venous stigmata," which are attributable to alcoholic excess, are commonly visible in cirrhosis at a very early period. By the time that ascites has *arisen the face has usually altered and has begun to assume a very characteristic appearance. It is thin and wasted, and the malar bones* are prominent; the eyes are somewhat sunken; the conjunctivæ are yellowish, and the complexion is sallow and unhealthy. The process of digestion is impaired, and absorption of nutritive material from the intestinal canal is diminished, so that there is a progressive loss of bodily strength with emaciation. The trunk and extremities are ill nourished, and at a late stage the attenuated frame offers a marked contrast to the swollen abdomen.

As the illness wears on, with progressive emaciation and increasing feebleness of voluntary and cardiac muscle, the patient is apt to show signs of poisoning, which are probably attributable to the increasing interference with the function of the liver. He becomes liable to epistaxis, to bleeding from the gums, and to purpuric eruptions on the trunk and extremities. Uncontrollable diarrhœa is also a common event, as in uræmia. Digestion is at a standstill, and he may thus sink from sheer asthenia, or may be hurried off by pulmonary inflammation. Often for some time before the end his mind may wander at night, perhaps also in the daytime. Occasionally a noisy delirium sets in; but more commonly the end is marked by apathy and increasing feebleness of body and mind, passing into drowsiness, coma, and death.

Course and Prognosis.—Owing to the obscurity of the early stages of the disease no accurate estimate of its total duration can be given. It is without doubt an extremely fatal disease, but evidence has been recently adduced to show that it is not so uniformly fatal as was formerly supposed; and many instances of recovery are alleged. The character of these alleged cures must be closely scrutinised. As regards some of them, it may be said that doubt attaches to the nature of the disease; in some the affection was probably of syphilitic origin, and the ascites, on which the diagnosis of alcoholic cirrhosis was mainly based had subsided on the absorption of the gummatous tissue in the liver.

At the same time it may be admitted that some patients suffering from undoubted alcoholic cirrhosis do lose their ascites, and do recover and preserve a fair measure of health for a considerable number of years. In one recorded case, where the diagnosis was confirmed by the supervention on separate occasions of mental symptoms and of peripheral neuritis, both clearly of alcoholic origin, the patient was in good health after repeated tappings, the first of which was performed some six years before (Bristowe). In another instance the patient was in good health after fourteen tappings, the first of which was more than three years before (Bristowe). A striking example is afforded by the case of a patient who recently died with contracted granular kidneys and pericarditis in St.

Thomas's Hospital. Twelve years before he had been a patient in the same place under the care of Murchison, suffering from alcoholic cirrhosis and ascites. From that date the patient, who had previously drunk freely, became a teetotaller, and during these twelve years he had been in fair health. At the post-mortem examination the liver was found to *weigh 59 oz., its capsule was much thickened and adherent to the diaphragm, the cut surface was that of a hobnailed liver, and the microscope* revealed the usual appearances of a multilobular cirrhosis. Further evidence on this point is perhaps afforded by the fact that cirrhosis of the liver is sometimes found unexpectedly in autopsies on patients who have died from some other cause.

It is clear, then, that in some few cases health may be restored after the appearance of symptoms of an alcoholic cirrhosis; but we must nevertheless believe that a positive cure is impossible. So far as present knowledge goes, the new fibrous tissue developed in the liver must persist in spite of all drugs and diets. The disease, however, may remain stationary, and if it be recognised at a very early stage, and alcohol from that moment be eschewed, the liver may undergo no further increase or contraction. The essential conditions of recovery in any degree are that the functions of the liver should be performed in a manner adequate to the maintenance of health, and that the portal blood should have free means of exit into the general circulation. Given these two conditions, it is probable that a fair degree of health may be maintained indefinitely, provided that no intercurrent disease, such as tuberculosis or renal disease, step in. But owing to the tendency of this new fibrous tissue to a steady and destructive contraction, long after the poisonous cause of its development has ceased to act, the conditions necessary for the restoration of health must be very rarely attained.

(*b*) **The unilobular form.**—*Morbid anatomy.*—This form of cirrhosis, which, though equally due to alcohol, is far less common than the other, is a very distinct disease, and presents many points of marked contrast with the preceding kind.

The liver is increased in size; as a rule it reaches a size and weight far beyond anything met with in the multilobular form. A weight of five to seven pounds is common; over ten pounds has been met with. The right lobe may measure thirteen inches in an antero-posterior direction, and may be more than six inches in thickness. During life its edge is commonly found to extend at least to the level of the umbilicus; it may descend much lower, and it often also stretches across the abdomen into the left hypochondriac region.

The natural surface is smooth, and herein is a great contrast with the preceding form. The capsule is often somewhat thickened, but there is seldom the degree of thickening, or of perihepatitis, met with in the multilobular form. Its normal shape and its sharp anterior edge are commonly retained, and there is no appearance of any tendency to contraction. The cut surface is also smooth. It may be of a mottled brown and white colour, due to the presence of a network of fibrous tissue throughout the organ which encloses the individual lobules of hepatic tissue. In many cases, however, where, as usually happens, jaundice has been present, the whole surface is of a yellowish or olive green colour. In consistence it is tough and hard, but it does not present the leathery hardness that is met with in the multilobular form previously described.

Microscopically a new development of fibrous tissue is seen throughout the organ; and this, with considerable uniformity, surrounds the individual lobules. It is for the most part, therefore, "unilobular" in distribution. Further, in many cases it may be seen to invade the lobules to some extent from the periphery, separating peripheral cells from each other and from the lobule, so that they come to lie stranded in the new tissue. It is richly or poorly nucleated according to its age and the activity of its development.

In nearly all cases a remarkable plexus of bile-ducts is seen embedded in the new tissue. In the neighbourhood of the portal vein, that is, in the centre of the triangular interlobular space where in health may be seen one or two small bile-ducts in transverse section, there are now seen one or more large irregularly-shaped spaces lined with columnar epithelium. Nearer the margin of the lobule, and more especially in the new fibrous tissue occupying the interlobular fissures, lie a series of smaller ducts which tend to be arranged around and parallel with the edge of the lobule; and of these ducts the lumen is much smaller and the epithelium lower and more cubical. From this system short lengths of duct commonly arise which come off at right angles, pass straight to the edge of the lobules, and apparently become continuous with columns of hepatic cells. These short ducts may have a well-formed cubical epithelium, but the lining cells usually show a tendency to become oval and to lie in the axis of the duct; moreover, the lumen of the duct is usually packed with detached cells, of a similar character, in a state of active proliferation. That all these epithelium-lined canals are in fact bile-ducts—not mere double rows of hepatic cells stranded in the new tissue—is shown by the fact that they can be readily injected from the hepatic duct, and they often (especially the smaller ones) show masses of inspissated bile in their interior.

The mode of origin of these new bile-ducts is somewhat obscure, and the matter has not been rendered clearer by its association with the problematic "biliary" form of cirrhosis. It is possible, though not likely, that they are a wholly new formation. Such a process would have no parallel in disease of any other organ. It has been maintained, again, that these ducts represent, and indeed are columns of liver-cells derived from the peripheral part of the lobule which is invaded by the new fibrous tissue; that their epithelium consists, in fact, of liver-cells degraded and converted into duct-cells. This view receives some support from the arrangement of the ducts, especially of the short ducts which run up to the margin of the lobule, where their cells become merged in those of the hepatic columns. On the other hand, if this were the true explanation, we should expect that a transitional stage would be met with, in which the process of conversion of the highly-organised liver-cell into the lowly duct-cell would be seen. But this is not the case. At the junction of lobule and duct there are liver-cells and duct-cells, but there are no cells in process of change from one form to the other. The explanation suggested by Cornil is perhaps the most satisfactory; his hypothesis may be briefly stated in these terms:—Where the liver tissue wastes from any cause, and the lobule thus grows smaller and its margin recedes, the biliary canaliculi, which in health lie inside the lobule, between adjacent rows of hepatic cells, are laid bare to view. In health these canaliculi are minute tubes formed only by a basement membrane; and it is to be supposed that, as they are left bare by the recession of the margin of the lobule, the epithelium of the extralobular bile-ducts multiplies and grows up into them, and tends to afford them a regular epithelial lining. In this way many facts are explained. In the first place, the usual arrangement and pattern of these ducts, which have been described above, become intelligible; secondly, these ducts, though far more common in this form of cirrhosis, occur under other conditions: they are not uncommon here and there in the multilobular form; they are common in the periphery of syphilitic scars; they may be seen around tubercles in the liver, and even in the lymphoid masses associated with leucocythæmia. The condition common to all these affections appears to be the destruction of the margins of lobules by the pressure of some kind of new formation. And it is clear that the development of these ducts has no relation to a previous biliary obstruction, as was formerly supposed; for they may be present in abundance in cases where there has been no suspicion of jaundice at any time. Finally, from the brilliancy of their staining capacity, we may conclude that the cells lining these ducts are in active life and growth, and in this respect they stand in marked contrast with the degenerate liver-cells into which they seem to merge. These epithelial cells are usually in a state of active multiplication, and, by their numbers, they may even occlude the lumen of the smaller ducts.

In conclusion, it may be stated that the difference between the multilobular and the unilobular form of cirrhosis appears to depend on the part of the portal system upon which the injurious influence of the alcohol first makes itself felt. In the former the morbid change may be clearly seen to arise around the main portal veins which lie in the triangular interlobular spaces or portal canals. In the latter there is evidence to show that the brunt of the damage falls rather on the small portal branches which approach each lobule from all points of its periphery; consequently the resulting new fibrous tissue is developed around each lobule, and by its encroachment upon the edge of the lobule an appearance of newly-developed bile-ducts may be produced. Finally, in view of the packing of the smaller of these new ducts with epithelial cells, it is possible to suppose that the common occurrence of jaundice in this form of cirrhosis is due to their occlusion by this means.

The problem of biliary cirrhosis.—It has been maintained that the appearances above described—namely, the unilobular development of a fibrous network which has numerous bile-ducts embedded in it—should, in some cases at any rate, be explained on the hypothesis that the primary disease lies in the bile-ducts, and that, as a consequence of this disease, the fibrous tissue is secondarily developed around them. In other words, a form of cirrhosis has been described, mainly by French observers, as "hypertrophic cirrhosis with chronic jaundice," or more shortly, as "biliary cirrhosis" as opposed to a "portal cirrhosis." There is considerable doubt, at any rate in this country, whether there be any ground for believing in the existence of a form of cirrhosis having a "bile-duct origin" as distinct from a "portal vein origin"; and, if an opinion is to be formed, a brief summary of the facts is necessary.

Laennec's cirrhosis, the alcoholic multilobular form here described, was well understood early in this century, and no other form was then recognised. So firm was the belief in the truth of Bichat's positive statement, "cet état (cirrhose) ne se complique jamais du volume extraordinaire du foie, au contraire il diminue," that if a cirrhosed liver were found increased in size it was supposed to be but an early stage of the small hobnailed liver. In 1859 Charcot and Luys pointed out that in some cases of cirrhosis, where the liver is large, the new fibrous tissue penetrates into the lobules and becomes "intralobular"; and this communication heralded the recognition of a form of cirrhosis distinct from the small granular form of Laennec. In 1874 Hayem published two cases of cirrhosis with enlargement, in which the individual lobules were similarly invaded by the new tissue, and in the same year Cornil described the appearance of new bile-ducts lying in the fibrous tissue. A year later Hanot published a thesis which established the existence of a form of cirrhosis, with permanent enlargement of the liver, which differs widely in its clinical and pathological features from the far more common small-sized form which, up to a few years before, had alone been accepted.

This form was described by Hanot as being characterised by a great enlargement of the liver, constant at all periods of the illness, by its smooth surface, and by the absence of evidence of contraction of the new fibrous tissue. He distinguished it, microscopically, by the unilobular and sometimes intralobular arrangement of the new tissue, and by the appearance in it of a plexus of small bile-ducts. He described its clinical features as a permanent jaundice without ascites, and without any evidence of portal obstruction, and a fatal progress due to the severity of the jaundice In the cases which had come under his observation he was unable to trace any one definite exciting cause. Some patients had resided in Algeria and had contracted intermittent fever. Other cases occurred in hard drinkers, but in others, again, no history of alcoholic excess could be elicited. No evidence was obtained of any connection with syphilis. While allowing that residence in a hot climate, malaria, and alcohol might play a part in the causation, he was inclined to attribute the disease to the spreading of an inflammatory process from the smaller bile-ducts, which he believed to be in a catarrhal state of unknown origin.

Charcot confirmed this clinical account and this view of a "biliary" origin. He was influenced by the identity between the anatomical appearance of this unilobular form of cirrhosis and that of the experimental form, which has already been mentioned as the result of the ligature of the common bile-duct in some lower animals. His train of reasoning led him to the conclusion that in the experimental form the cirrhotic process started around the small bile-ducts, and was due to the catarrh excited in them by the stagnation of the bile; and he applied this conclusion to explain this form of cirrhosis in man.

The evidence on which this theory of a biliary origin of these cases was based has failed on further investigation. It is known now that the results of experimental ligature of the common bile-duct cannot be applied to man, and that little or no cirrhosis ever follows prolonged obstructive jaundice. The appearance of new bile-ducts, on which so much stress was laid, is now known to be a phenomenon of common occurrence in many forms of liver disease which are unattended by jaundice. And the microscopical evidence of the catarrhal condition of these ducts, on which the theory was partly based, is exceedingly doubtful

The account of the morbid anatomy and of the clinical features, as given by Hanot and Charcot, is in the main identical with that of the unilobular form of alcoholic cirrhosis already detailed. In nearly all (if not in all) such cases occurring in this country there is a history of hard drinking. Osler in America states that all the instances he has met with have been in hard drinkers. And the undetermined point at issue is whether any cases of unilobular cirrhosis own any cause other than alcohol, or possibly malaria; and whether any of them can be referred with probability to a primary morbid change in the bile ducts.

Symptoms.—The clinical features of this form of cirrhosis are very different from those of the multilobular form (*a*) already described (p. 173), and this difference depends partly upon the anatomical arrangement of the new fibrous tissue It may be said generally that in this form there is a great tendency to severe jaundice and little or no evidence of portal obstruction.

It is probable that the disease may be well advanced before the patient comes under notice. Some sudden disorder usually brings him under examination, and the liver is then found much enlarged. The early symptoms do not amount to more than some general failure of health, loss of appetite, slight weakness, and perhaps a sensation of weight in the right hypochondrium. Sometimes the patient has vaguely noticed that his abdomen is growing larger Of the duration of this early period we have no certain knowledge; but it is probable that a year or more may elapse before such patients come under observation

In many cases it is the onset of jaundice which causes alarm; and in most instances jaundice is present, sooner or later. It may, however, be entirely absent, but patients in whom this has been noted have usually died at an early period of the disease. The jaundice is commonly intense, but there is some doubt whether bile is ever entirely absent from the stools. When once established it commonly persists till death.

Ascites is either entirely absent or so slight as not to need interference; and there is no direct or indirect sign of portal obstruction in the form of dilated veins or hæmatemesis.

The spleen is either normal or but slightly enlarged. The large, hard, smooth liver is readily recognised, as it occupies a large part of the abdomen, and often produces a visible enlargement of it and also of the lower thoracic region on the right side; its edge is to be felt at least on a level with the umbilicus, and it may extend into the right iliac fossa.

An important feature of this disease is the occurrence of fever. There is often an evening rise of temperature, and this occurs far more commonly than in the multilobular form. In many cases, however, the fever is high: it may range from 102° to 104° for considerable periods, especially towards the termination of the illness, and it may also assume a hectic course suggestive of hepatic abscess or pylephlebitis.

The urine is said commonly to show diminution of urea; certainly *this is not always the case. Leucin and tyrosin have occasionally been found in it. Diarrhœa is common and towards the end may be* uncontrollable, resembling that met with in chronic uræmia. The facial aspect of the patient has something of the appearance seen in the multilobular form; and in long-standing cases there is progressive emaciation and increasing feebleness. The ending is often sudden and acute: the temperature rises, the tongue becomes dry, the pulse rapid, petechiæ may appear on the skin, the condition during the last few days of life has a close resemblance to that observed in acute yellow atrophy of the liver, and the patient dies comatose.

The duration of life after the first recognition of the malady is very variable. In many instances the patient dies within the first year; but cases have been recorded where life had been prolonged for five and even seven years

Complications of alcoholic cirrhosis.—Other affections due to alcoholic excess, such as delirium tremens, chronic alcoholic insanity, or a peripheral neuritis, may coexist with cirrhosis of the liver.

Slight albuminuria is of common occurrence, being sometimes attributable to the pressure of ascitic fluid on the renal veins. A chronic interstitial nephritis is found in about 15 per cent of patients dying from cirrhosis; a chronic tubal nephritis in a much smaller proportion.

Thrombosis of the portal vein is a rare complication which adds materially to the rapidity of accumulation of ascitic fluid and to the gravity of the illness.

An important complication, which is probably an indirect result of the alcoholic excess and the attendant loss of resisting power, is the supervention of tuberculous infection. Occasionally a definite tuberculous phthisis arises, recognisable during life. Sometimes old caseous foci, cavities, or scarring are found at the apex of a lung at the autopsy. But the tubercle is more commonly of the gray miliary form, affecting the peritoneum, or the pleura, or both membranes. In not a few cases an abundant crop of gray tubercle is found on the peritoneum and on the surface of the liver; and a pleuritic effusion occurring on one side, especially if the fluid on withdrawal is found to be blood-tinged, is always strongly suggestive of a tuberculous origin.

B. Malarial cirrhosis.—The connection between cirrhosis of the liver and malaria is generally admitted; but, looking at the frequency of occurrence of the various forms of malaria in different countries, a cirrhosis of this origin cannot be said to be common. In this country, although the victims of chronic malarial cachexia are fairly numerous, a pure malarial cirrhosis is very rarely met with. The evidence derived from countries where malaria is endemic is seldom precise as to the anatomical details of the hepatic change. And, further, it must be remembered that in many reputed cases of malarial origin, due to residence in hot climates, the history of the patient cannot be cleared from the suspicion of alcoholic excess; it is not improbable, therefore, that even in such cases alcohol does often play an important part in originating the disease.

There is evidence, however, to show that a cirrhosis may supervene upon that condition of the liver which is commonly described as chronic engorgement. Hyperaemia of the liver is a general and important feature of malarial fever. Repeated attacks of such fever, while leading, on the one hand, to a general malnutrition or malarial cachexia, tend also to produce a state of chronic congestion of the liver, or, to use the term employed by Kelsch and Kiener, of "*hyperémie phlegmasique*." In this condition the liver is enlarged, it commonly extends downwards to the level of the umbilicus, and is found to weigh four or five pounds. It is of firm consistence, dark red in colour, and bleeds freely on section. The natural and cut surfaces are smooth. Microscopically such a liver shows an intense and general hyperaemia, to which probably the increase in size is largely due, and in the connective tissue which supports the portal veins an increase in the number of nuclei is to be observed.

This stage, which is of common occurrence, is well within the limits of recovery. In a small proportion of instances, however, it is the forerunner of a definite cirrhosis. Of the cirrhosis thus induced both the multilobular and the unilobular kind are met with. Each form, moreover, is attended by the same train of symptoms in the malarial as in the alcoholic disease, and no special description is needed.

On the one hand, the patient may present all the symptoms of the common form of alcoholic cirrhosis, and the liver may turn out to be of the small hobnailed variety. It is in such cases more particularly that the possibility of alcohol as an important additional factor cannot be excluded altogether. On the other hand, many cases of the unilobular kind have been recorded which are of much purer malarial origin. The liver remains enlarged; it is firm and resistant; there is little tendency to contraction of the delicate fibrous network which may be seen to infiltrate it, and ascites is accordingly absent or slight. Considerable enlargement of the spleen is nearly a constant coincidence. Jaundice is comparatively uncommon, but it may appear and may assume *great severity. Finally, in these cases there is a tendency to lardaceous degeneration of the liver which has no parallel in the* corresponding alcoholic affection.

C. SYPHILITIC CIRRHOSIS.—Of all the abdominal viscera the liver is most liable to syphilitic affections. The gumma and its resulting cicatricial tissue are met with both in acquired and in hereditary syphilis, but in the hereditary form of the disease there occurs also a peculiar form of cirrhosis, which is probably not developed under any other conditions, and which requires separate description. It is extremely doubtful whether syphilis is ever responsible for either of the two anatomical varieties of cirrhosis already described. Syphilitic changes are as a rule quite distinctive and easily recognisable.

Morbid anatomy.—The starting-point of the fibroid change associated with acquired syphilis is undoubtedly the development of the gumma, though gummata do not in all cases lead to anything worthy of the name of cirrhosis. The gumma may occur singly, but commonly there are many; and a score or more, varying in size from a pea to a Tangerine orange, may be found scattered throughout the length and breadth of the organ. They may occur in any part of the liver, superficial or deep, but there is a clear tendency to their development at the junction of right and left lobes, beneath the suspensory ligament and in the neighbourhood of it. They are often recognisable during life in this situation, and they are also often found unexpectedly in the post-mortem room. When seen in this way they are usually dead-white or grayish white in colour, according to the degree of caseation; they are roughly spherical, and often fused together into large lobulated masses. Microscopically the central part shows nothing but caseous material, and it is rare to find much trace of the original cellular structure of the gumma. Around the central caseous area there is a zone of new cicatricial tissue which has a degree of cellularity varying with its age, and from this zone short fibrous bands may be seen to radiate for a short distance into the liver tissue. In this stage the gumma is of no great clinical importance, and, as a rule, grave results do not ensue unless certain subsequent changes set in.

The natural end of the gumma is caseation with complete or incomplete absorption, and replacement by fibrous scar tissue. And it can be understood that the final result upon the liver will vary greatly according to the position, extent, and number of the gummata which undergo this change. Two extremes must be considered, between which all grades of severity may be met with. In the mildest degree of the affection, when the gummata have been small and superficial, a few scars puckering the surface of the liver, and perhaps a little thickening of the peritoneum around, may be the only marks of this occurrence. Each scar, on vertical section, will show a wedge-shaped area of cicatricial tissue extending into the liver substance for a depth of one-third or half an inch, and perhaps also microscopical examination will reveal in it a small central speck of unabsorbed caseous material. As I have already stated, well-formed bile-ducts *are often seen in such scars. In the opposite extreme, in which* the affection is far more grave, the liver is grossly deformed. In these cases there have been numerous gummata scattered throughout the whole or a large part of the organ—some separate, some fused into large masses, some superficial, some deep. And it results from their invariable ending in caseation and cicatrisation that the whole or a large part of the organ is seamed and traversed in all directions by broad fibrous bands, which on section are seen to separate large irregular masses of liver tissue. According to the stage at which the process has arrived, these bands may or may not still enclose caseous foci visible with the naked eye. In consequence of their contraction the surface of the liver may be scarred and furrowed, or it may come to present rounded eminences separated by deep depressions, or it may become largely lobulated, so that its appearance has been compared to that of the kidneys of young animals. Sometimes the depressions on the surface are so deep and close that the intervening and protruding portions of liver tissue become almost polypoidal in form. There is also commonly, but not invariably, some degree of general inflammatory thickening of the peritoneal covering of the liver, which may be firmly adherent to the diaphragm and surrounding structures.

Before this severe degree has been reached there has been, undoubtedly, considerable destruction of liver tissue by the compression of these contracting fibrous bands. But, with the exception of the local atrophy thus produced, the bulk of the tissue of the organ shows no change; the vessels are free, and the connective tissue of the portal canals is unaltered. There is a tendency, however, to the supervention of lardaceous degeneration, and cases have been met with where both alcoholic excess and syphilis have been in operation, so that gummata and this localised fibroid change have been found in coexistence with a genuine granular cirrhosis.

Such gummata, with scarring and lobulation of the liver already described, are also met with, though rarely, as a result of hereditary syphilis, and need no further description.

Another form of disease, distinctly due to hereditary syphilis, is a diffuse interstitial hepatitis, often found in still-born children, sometimes in children who have survived their birth for weeks or months; rarely in children beyond this period. The liver is uniformly enlarged, heavy, and hard, smooth on the natural and on the cut surface, exsanguine, and pale or reddish gray in colour. Its lobular structure is indistinct; to the naked eye it may show no resemblance to liver tissue. It may be mistaken for a lardaceous liver. It is found microscopically that some stage of an interstitial hepatitis is in progress. The whole organ from end to end is packed with formative cells and developing or fully-developed fibrous tissue, which affects not only the portal canals, but invades the individual lobules, not only separating the columns of hepatic cells from each other, but even separating the individual cells from their neighbours. So that in an advanced example there will be seen single liver-cells or groups of cells, still recognisable as such, scattered about in a matrix of developing or fully-formed fibrous tissue; and no trace of the normal lobular arrangement may remain. Rarely miliary gummata are also found to be present, and sometimes a lardaceous change may be displayed by suitable staining methods.

The symptoms of the interstitial hepatitis due to hereditary syphilis are not clearly known, and the condition is scarcely recognisable during life. But the liver may be recognised as enlarged; and jaundice and some degree of ascites have been observed.

On the other hand, the recognition of gummata in the liver, whether in children or in adults, is of the greatest importance. The liver is often slightly enlarged, either as a whole or more particularly that part of it which presents in the epigastrium. In many cases the projection of one or several gummata may be felt in this region upon the surface; and occasionally one large gumma as large as a Tangerine orange may be palpable. Sometimes no symptoms whatever are produced, and the hepatic condition is discovered accidentally. There may, however, be a sensation of weight in the right hypochondrium, or even some degree of pain, presumably due to implication of the peritoneal covering, and it may be some such sensation which first brings the patient under observation. Unless the portal vein or one of its large branches be interfered with by the development of gummatous tissue around it, the general health, as a rule, is but little disturbed. A very important though rare phenomenon is the occurrence of fever. In one recorded case of a boy, who presented traces of old interstitial keratitis, the appearance of a large apparently solitary gumma in the liver was accompanied by a daily rise of temperature to 102° or 103°, in hectic fashion, for a period of many weeks. The fever subsided and disappeared within a day or two of the commencement of treatment by potassium iodide (Bristowe). A trace of such fever has been known to occur in connection with hepatic gumma in the adult.

As the fibroid change sets in and the gumma gives place to cicatricial tissue, any further development of symptoms will depend entirely on the position and extent of the change. The portal vein, or some of its large branches within the liver, may chance to lie in the grasp of the contracting fibrous tissue. There ensues, then, all the train of phenomena which have already been described as marking portal obstruction: ascites, hæmatemesis, the external appearance of dilated veins, and grave interference with the digestive functions of stomach and intestine. By similar interference with the main hepatic bile-ducts jaundice may be produced, but it is a far less common occurrence than ascites. It follows that the alcoholic and the syphilitic forms of the disease may be indistinguishable by their symptoms alone. Gummata, however, may be definitely felt in the epigastrium; or there may be a history of syphilis and no history of alcoholic excess. And in young subjects all evidence of hereditary syphilis must be sought for, in skin, teeth, eyes and bones.

Treatment.—A rational plan of treatment will be founded, in the first place, on a knowledge of the cause of the cirrhosis; and in the second place, on an appreciation of the exact manner in which the disease produces impairment of health and a tendency to death.

In all cases, whatever the cause, alcohol must be strictly avoided, though occasions may arise in a late stage of the disease when its temporary use may be called for. If there is reason to believe that malaria has played a part in the causation, the choice of residence in a suitable locality, either at the seaside or at a bracing moderate altitude, is of the first importance If there be direct evidence that the disease is of syphilitic origin, or if indeed there be any suspicion that the disease is not of the ordinary alcoholic form, a trial of potassium iodide, with or without mercury, is the correct course to pursue. The prognosis is certainly less unfavourable on the whole in the syphilitic than in the alcoholic disease; but this difference is present only in the early or gummatous stage. By the timely use of antisyphilitic remedies the growth of gummatous tissue may be checked and its complete absorption materially hastened; so that symptoms derived from interference with portal vein or bile-duct may subside in an early stage and may not recur. Instances of such a happy result have often been recorded. But if the fibroid condition be already advanced, and if symptoms due to the contraction of broad fibrous bands traversing the liver have set in, there is no evidence to show that any drug can be credited with the power of arresting the disease; and as regards the probability of recovery, the syphilitic and alcoholic forms are from this stage forward on a par.

As concerns the management of the patient, the regulation of his daily life, and the handling of the various symptoms that may arise, all forms of cirrhosis may be roughly grouped together The diet must be plain and simple; it should be ample for the maintenance of strength, while excess must be carefully avoided. At the beginning of treatment milk should form the main (if not the only) article in it. From three and a half to four pints a day may be given to an adult, in various ways according to taste; slightly diluted with some alkaline water, or as a jelly, or in the form of a milk soup containing some vegetables. It is well to avoid meat entirely for a time, or at any rate to allow only white meat or fish in small quantities. All meat, broths and soups may well be discarded, unless their temporary stimulant effect be required. Vegetables and fruit may be allowed, those kinds being preferred which contain least starch. And, as a general rule, it is well to reduce all forms of starchy and saccharine food to a minimum in view of the state of the stomach and the proneness of these substances to undergo fermentation.

If possible, complete rest and plenty of fresh air should be secured for these patients.

In the matter of drugs, the limits of the use of potassium iodide have been laid down already. And it is reasonable to believe that in the general medicinal treatment the use of acids, bitter tonics, and, sometimes, the milder preparations of iron carries us as far as we can go. Bismuth and magnesia are often of use in allaying the tendency to vomiting produced by the catarrhal condition of the stomach; and thymol serves sometimes to check the flatulence which is commonly troublesome. There is no doubt that diuretics, such as digitalis, squill, copaiba, and diuretin, which have received ample trial and recommendation from time to time, do in some instances ensure the passage of an increased amount of urine, even so far as to promote a perceptible diminution of the ascites. Though such a treatment is probably harmless it is too often useless, especially in cases of extreme ascites where the diminished secretion of urine is attributable to pressure on the renal veins. Perhaps the most satisfactory diuretic to be used in such a case is the well-known combination of mercury, digitalis, and squill.

The propriety of attempting to remove ascitic fluid by powerful purgatives is still more questionable; but this method of treatment was at one time generally practised. It is of course well to ensure free daily evacuation of the bowels by the matutinal use of saline aperients, such as Carlsbad salts, but anything more drastic than this is certainly not to be recommended.

Our views as to the expediency of paracentesis have undergone modification in the last few years. The operation was formerly regarded as a last resource, and was consequently looked upon as the herald of death. Increased experience has led to its extended adoption at a much earlier period of the disease; it should undoubtedly be employed whenever much discomfort is produced by the ascites, and more especially whenever there is any marked degree of upward pressure upon the heart or lungs.

The occurrence of hæmatemesis, however slight, must be taken as the signal for absolute rest of the body as a whole, and especially of the stomach and adjacent part of the œsophagus. All food by the mouth must be forbidden, and, at any rate during the few days of danger, the patient must be kept entirely on rectal feeding. It is extremely doubtful whether ergot or ergotin is of any avail: the use of nitrite of amyl has been suggested on definite grounds. But opium, preferably as the hypodermic injection of morphia, is certainly of indirect value in calming the patient and allaying his anxiety.

Diarrhœa is apt to be intractable. Although the attendant loss of fluid from the portal area is at any rate not harmful, yet the passage of the contents of the bowel is at the same time so hurried that absorption of nutritive food-products is imperfect. Gastric digestion and absorption being already at a low ebb, this diarrhœa has a disastrous effect, and in many instances it is the beginning of the end. The subnitrate or salicylate of bismuth in large doses is perhaps the most efficient means of coping with it; the mineral acids, catechu, and the strong preparations of iron, such as the pernitrate, may also be tried; but opium is seldom safe at this stage of the disease. In many cases all treatment fails to check it.

In conclusion, when the use of alcohol has been effectually stopped, a satisfactory diet enjoined, and a regular action of the bowels established, it remains to deal with such complications as ascites, hæmorrhage, diarrhœa, and pleuritic effusion. But whether the individual patient will succumb, or whether he is to be one of that small number in whom the symptoms disappear, is beyond our knowledge, yet the result will depend largely on the stage of the disease at which treatment was begun.

In conclusion I may mention a rare combination of cirrhosis with (so-called) adenoma, described by Dr. Kelynack and others; but as the disease has no clinical importance I need do no more than refer the pathological reader to Dr. Kelynack's paper which is indexed below in the list of references.

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REFERENCES

General Literature

1 Brieger *Virch Arch* Bd lxxv Heft 1 2 Bristowe *Brit Med Journal*, April 23, 1892 (Prognosis).—3. *Brit Med. Journal*, November 19, 1892 (Discussion on Prognosis and Treatment) —4 Charcot *Leçons sur les Maladies du Foie* —5 Cornil and Ranvier *Manuel d'histologie pathologique* —6 Frerichs. *Clin Treatise on Diseases of the Liver*. New Syd Soc 7. Goodhart *New Syd Soc Atlas*, fascic. 4, 1882 —8 Green *Trans Path. Soc* 1876 —9. Laennec *Traité de l'auscultation médiate*, t ii p 501 —10 Lancereaux *Atlas d'anatomie pathologique* —11 Price *Guy's Hosp Reports*, 1881 —12 Sappey *Mém de l'Acad de Méd* xxiii 269 —13 Taylor *Trans Path Soc* 1879 80 14 *Trans Path Soc* 1889 (Discussion on Morbid Anatomy and Pathology of Chronic Alcoholism) 15 White, Hale *Guy's Hosp Reports* 1882 —16 Wilson and Ratcliffe *Brit Med Journal* Dec 27, 1890

Special Literature

Malarial Cirrhosis · 17 Davidson *Hygiene and Diseases of Warm Climates* 18 Kiener and Kelsch *Arch de Phys norm et path* 1878, 1879 19 Lancereaux *Loc cit.* **Biliary Cirrhosis**: 20 Clarke, Michell *Brit Med Journal*, May 3, 1890 21 Charcot and Gombault *Archives de Phys* 1876 (two papers) 22 Hanot. *Étude sur une forme de cirrhose hypertrophique du foie*. *Thèse de Paris*, 1875. 23 Legg, W. *St Bart. Hosp Reports*, 1873 —24 Saundby *Trans. Path. Soc* 1879 25 Sharkey. *St. Thomas's Hosp. Reports* 1888 **Cirrhosis associated with Tuberculosis**: 26 Hanot and Gilbert. *Compt rend Soc de Biol* 1890 and 1892. **Connection of Cirrhosis with specific Fevers** · 27 Botkin *Berl klin Wochenschr*. 1872, No 22 —28. Joffroy. *Brit. Med Journal*, April 23, 1892 29 Kelly. *Trans. Path. Soc*. 1877. 30 Pepper *Journal Amer Med Assoc* July 2, 1887. **Cirrhosis and Adenoma**: 31. Kelynack *Edinb Med Journal* 1897, p 187

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TUMOURS OF THE LIVER[1]

Secondary cancer of the liver is by far the most common form of tumour. Thus, I find that in the Clinical Reports of the Medical Wards of Guy's Hospital during the years 1888-1893, both inclusive, there were admitted 58 cases diagnosed at the bedside to be cancer of the liver, of which certainly not more than two or three were primary; 15 cases of syphilis of the liver; 12 of abscess; 12 of hydatid, and 7 of sarcoma. The frequency with which secondary cancerous deposits take place in the liver is shown by the fact that at Guy's Hospital, during the years 1885-1893, both inclusive, out of about 4200 post-mortem examinations 136 examples of secondary deposits in the liver were met with in the dead-house, and of these at least 126 were carcinomatous, that is to say, secondary carcinomatous deposits are found in the bodies of 3 per cent of all persons who die in Guy's Hospital, a percentage which exactly coincides with that given by Leichtenstern. Further, I find that of all persons in whom at death malignant disease of any organ is found, about 50 per cent have secondary deposits in their liver.

So many of the symptoms of cancer of the liver are due to physical alteration in shape of the organ that it will perhaps be best to describe first the morbid anatomy.

Morbid anatomy.—If the patient die soon from the effects of the primary growth, the secondary deposits found in the liver may be few and small; but, inasmuch as the primary growth is usually in some organ, the blood of which is returned by the portal vein, the hepatic tissue often becomes affected early; and in many instances, therefore, there is an enormous deposit of cancer in the liver by the time of the patient's death. Cancer causes the liver to be heavier than any other disease of it; in the last case under my care the liver weighed nineteen pounds, and even heavier livers have been recorded. The secondary deposits take the form of whitish nodules scattered about irregularly in the liver substance, suggesting, by their distribution, that we are correct in believing that cancer elements are conveyed in the portal blood to the liver, and multiply wherever they may happen to be deposited. At the patient's death all the nodules are not of the same age, and they are of various sizes, from those which require a microscope for their detection to those which are as large as a fœtal head. In a marked case the organ has bosses all over it, especially perhaps on its upper surface. The older of these are umbilicated, and often there is a little local thickening of the peritoneum over them. The nodules, which at first are more or less globular, grow most easily in the direction of least resistance, and this, to some extent, may explain the fact that cancerous nodules are usually absent from the interior of the liver unless some are also visible under its peritoneal coat. The nodules destroy the hepatic tissue, but they increase more rapidly than they destroy; hence the enormous weight of the liver in an advanced case. Gradually those which are contiguous coalesce; so that, on section of the liver, large *irregular white masses of various shapes, and rounded nodules, occupying, it may be*, several cubic inches, are seen let into the hepatic substance, as it were, which is dark by contrast. This striking contrast is often much enhanced by the bright yellow tint of the growth, due to staining by the bile, the dark red due to hæmorrhage, and the pale yellow due to fatty degeneration.

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[1] These will be considered in the order of their clinical importance.

There is no special alteration to describe in the hepatic tissue itself. The cancer as it grows causes atrophy of the hepatic cells; hence, even when the liver is very heavy, there is much less hepatic tissue than normal; what is left appears, however, healthy except that the cells in immediate contact with a cancerous nodule are compressed. Although the growth cannot be shelled out from the hepatic tissue, the demarcation between cancer substance and liver substance is very sharp. Injection experiments have shown that blood-vessels from the hepatic artery grow into the cancerous growth along its septa. The growth resembles that of the primary seat of the disease; hence its consistency, its tint, and the amount of juice obtained by scraping it all vary. After they have attained a certain size the nodules begin to degenerate in the centre, the part farthest removed from the blood-supply. The cancer cells may become fatty and break up, and, consequently, the centre of the nodule becomes yellow, soft, and of the consistency of batter, and if, as sometimes happens, much of the stroma has softened, most of the growth may be washed away with a stream of water, so that a ragged, shreddy mass of stroma is left behind. The fibrous tissue of the cancer, however, usually contracts as time goes on; and as this contraction is most marked in the centre, where softening has been greatest, the growth when on the surface of the liver becomes umbilicated. The process of softening sometimes lays open the blood-vessels of the stroma, especially in those rapidly-growing tumours which are from the first red and vascular. Thus considerable hæmorrhage may take place into the cancer, which becomes a soft, dark red mass; and it may even extend into the substance of the liver itself. Sometimes, under these circumstances, the liver may clinically be found to enlarge very rapidly; and in rare cases hæmorrhage has taken place from a nodule on the surface, and blood has poured into the peritoneal cavity. Often the new growth undergoes yellowish, cheesy degeneration; and sometimes also a quantity of clear fluid collects in its interior and replaces the atrophied cells, which have become absorbed. Usually some bile-ducts are compressed by the new growth in their course through the liver, which, consequently, becomes stained here and there of a deep yellow colour; this colour often extends into the cancer masses themselves, and the growth of these into the veins, which is a very common event, leads to considerable ante-mortem clotting in them.

A cancerous mass may envelop and infiltrate the gall-bladder, but often when this appears to have happened the growth has been primarily in the gall-bladder, and has affected the liver secondarily. In the same way, when, as is not uncommon, a malignant mass is seen to implicate both the pylorus and the liver, the stomach should be regarded as the primary seat. Sometimes cancer of the liver grows directly into the diaphragm, which thus becomes adherent; and I have seen prominent nodules on the surface of the liver leading to the growth of cancerous nodules on the peritoneal lining of the abdominal wall at the spot in contact with the hepatic growth this has occurred even when no adhesions between the liver and the abdominal wall have taken place, but, on the other hand, I have known the adhesions so firm that the liver did not move up and down with respiration, and at the autopsy some of the anterior abdominal wall had to be taken away with the liver in order to remove the organ.

The growth in the liver often leads to the formation of a malignant nodule at the umbilicus, and in such a case I have seen the whole of the round ligament converted into a cancerous cord. If the growth has been long present in the liver, or if the organ which is the seat of the primary cancer returns its blood into them, the glands in the transverse fissure will be secondarily enlarged, even to the size of a hen's egg Their pressure on the common bile-duct leads to distension of the gall-bladder, converts the mottled bile-staining of the liver into a deep yellow staining of the whole organ, and the jaundice of the entire body becomes extreme and persistent If the cystic duct be compressed, so that no bile can reach the gall-bladder, the latter is found contracted and contains a little mucus only. It is rare for the growth to spread to the suprarenal capsules, kidney, duodenum, or colon. As the secondary cancers of the liver repeat in every particular the histological characteristics of the primary growth, it is unnecessary to give a description of their microscopical appearances, which will be found in treatises on pathology

It is not unusual to find gall-stones in the ducts or gall-bladder, and consequent dilatation and ulceration of the bile passages may occur Sometimes the gall-stone by its irritation has set up a primary growth of the gall-bladder or the ducts. It is outside our subject to describe the post-mortem appearances of the primary growth in other organs, the secondary deposits elsewhere than in the liver, the bile-stained condition of the body generally, and the post-mortem signs of death from cancer It is worth while, however, to point out that secondary cancerous deposits usually take place by the agency of the lymphatics and not by the venous system, and are conveyed by the portal vein; and that probably the reason why secondary deposits in the liver are so common, is that the primary growth, being out of reach of surgical interference, goes on to ulceration. peripheral twigs of the portal vein are thus laid open, and infection of the liver takes place by this vein.

Although a colloid cancer of the liver, secondary to colloid cancer elsewhere, repeats the appearance of the primary growth, colloid cancer invading the liver by direct extension from the peritoneum has, according to Schueppel (*Ziemssen's Encyclopædia*), quite a different appearance; for the invasion takes place by the lymphatics, and thus we see at first numerous subserous rows of colloid material, and later, these appear to run through the liver like colloid strings. Ultimately the organ may thus become one mass of colloid material.

Symptoms.—In more than half the cases the deposit of cancerous *nodules in the liver produces no symptoms by which they can be recognised during life, and then, as far as we know, they do no harm.* If the secondary growths in the liver do produce symptoms, those of the primary growth will exist side by side with those of the hepatic affection. The stomach, which is the seat of the primary growth in more than a quarter of all the cases, the gall-bladder, rectum, and pancreas are each a common source of cancer of the liver. The great frequency of cancer of the pelvic organs and breasts of women explains the fact that the proportion of males to females that die with cancer of the liver is as 3 to 4.

In about half the cases in which the liver is obviously affected, the seat of the primary growth cannot be discovered during life, then it is often found after death in the pancreas, and usually in the head of this organ.

In the following account I shall omit all reference to symptoms due to the primary growth, or common to cancer in any part of the body. The ages of 75 per cent of all patients with cancer of the liver are between forty and seventy years; rather under 20 per cent are under forty, and rather over 5 per cent are over seventy. Hepatic cancer is all but unknown under twenty.

The symptoms by which we can recognise secondary cancer in the liver are as follows—Both by percussion and tactile examination enlargement of the liver can usually be made out. It may reach far below the umbilicus, the hepatic dulness may be increased upwards in the mid-axillary line as far as the fifth rib, and on the left side it may blend with that due to the spleen. The edge of the enlarged organ can nearly always be felt to move up and down with respiration, and, as Sir William Jenner remarks, it often appears lower during life than in the post-mortem room, for as the last respiratory movement is expiratory, it is drawn up at death as high as possible. It is quite common, when the patient becomes much wasted, for movement of the enlarged liver and outward bulging of the right lower ribs to be easily visible. The edge feels hard, and, owing to the presence of several carcinomatous nodules, is often irregular. the nodules can be felt also on so much of the upper surface as comes below the ribs, so that the whole organ feels irregular, knobby, and hard.

In rare cases the nodules can be made out to be umbilicated, and if this be ascertained it is absolutely diagnostic of cancer: occasionally, if they are either growing or degenerating very rapidly, they are soft, and give an obscure sense of fluctuation. Sometimes, too, a rub can be both felt and heard over the liver. This indicates either some local peritonitis, or the presence of a cancerous nodule in the parietal peritoneum against which a cancerous nodule in the liver is rubbing. Before deciding that a liver is not carcinomatous, the patient should always be made to take a deep inspiration, for this may reveal a nodule that would otherwise remain hidden under the ribs. Sometimes the cancer grows so fast that the enlargement of the liver may be watched from week to week; and occasionally the whole organ enlarges even more rapidly, and individual nodules may become more prominent within a day. This is very strong evidence in favour of cancer, and indicates considerable hæmorrhage into the liver. In a few instances the nodules slowly get smaller, as they undergo degeneration.

There are certain rare cases in which the new growth infiltrates the whole liver, which is then enlarged and hard; but no nodules can be felt

Another important sign is tangible distension of the gall-bladder, which appears as a rounded tumour at the lower edge of the liver, and indicates that secondarily enlarged glands are pressing on the common duct. It has already been mentioned that the umbilicus is often affected, and during life it may be hard and enlarged.

The patient usually, but by no means always, complains of pain in the region of the liver, both back and front, due probably to stretching of the capsule or to some local peritonitis, and, especially when this has occurred, the organ is tender, and he suffers from a cutting pain when he coughs. Pain is often referred to the right shoulder-joint, a point of considerable diagnostic importance. I have had but little experience to show whether the localised cutaneous tenderness which Dr. Head has shown to be associated with visceral disease is of much importance in cancer of the liver. Probably not, for the patients are very ill and weak, and the tender areas due to the primary disease may well overlap those due to implication of the liver. When the liver is very large the patient experiences a sense of fulness and dragging in the right hypochondrium.

About half the patients who during life present symptoms of carcinoma of the liver are jaundiced; and this nearly always means that enlarged carcinomatous glands in the transverse fissure are pressing on the common bile-duct: but in some cases the pressure is due to the primary growth, especially if it be in the head of the pancreas; and occasionally enough of the hepatic ducts in the liver may be compressed by nodules of new growth for jaundice to appear. Or there may be primary cancer of the bile-ducts (p. 208). It is extremely important to bear in mind that by far the most frequent cause of long-standing jaundice is cancer of the liver, which also produces deeper jaundice than any other common disease; thus patients suffering from cancer present, in the most extreme form, those symptoms due to circulation of bile in the blood and to its absence from the intestines. The jaundice, too, is permanent; the only exceptions to this rule are those excessively rare cases in which, although the patient has cancer of the liver, the jaundice is due to a gall-stone in the common duct, which is either passed on or slips back. The skin, deeply and slowly stained by bile, gradually becomes more and more green, and ultimately assumes a peculiar earthy dark green tint, which, especially if the patient be aged and wasted, is almost diagnostic of cancer of the liver. The other effects of bile in the blood are also evident. The urine is very dark and has a yellowish froth, the numerous scratch marks show the intense pruritus, the bitter taste in the mouth is very unpleasant, the sweat may be bile-stained, and if, as often happens from secondary deposits in the lungs, the patient gets bronchitis or pneumonia, the expectoration may be yellow. Sometimes the pulse is slow; in rare cases the patient may complain of xanthopsy, and occasionally patches of xanthelasma appear. The usual cause of death is bile poisoning, or cholæmia as it is named. In such cases, although the end may be rapid, usually the patient gradually becomes more and more drowsy, with in rare cases an occasional convulsion; day by day his coma slowly deepens; his breathing becomes shallower and shallower; at last he cannot be roused, and sometimes for days before he passes away a superficial observer might think that death had already taken place. There are few things more characteristic in medicine than to see an aged gray-haired patient extremely wasted, with dry, dark green skin hanging in loose folds, lying perfectly still, so drowsy that he is more dead than alive. If we turn down the bed-clothes the liver may be seen deforming the shape of the abdomen; and it will be noticed that the sheets are stained yellow, either from urine or sweat. The absence of bile from the intestine causes indigestion and constipation, the motions are pale, they smell horribly, and contain much undigested fat.

Authors differ as to the frequency of ascites. For my own part, I think that it is not so common as jaundice, and that it usually comes on late in the case. It may occur with or without jaundice, the two being associated in only about 20 per cent of all cases of cancer of the liver diagnosed as such during life. The fluid is clear, it is often stained yellowish green by bile, and, if any of the superficial hepatic growths have bled, it may contain blood. Inasmuch as ascites may be absent when there has been considerable pressure on the common bile-duct to which the portal vein lies so near, it seems reasonable to doubt whether it is due to pressure on this vein; especially as I have elsewhere (p. 120) brought forward evidence to show that in perihepatitis, in which disease ascites is often such a prominent feature, it is probably due to chronic peritonitis. I think carefully-made autopsies will show that in many cases at least of cancer of the liver in which ascites is present there is also chronic peritonitis due to malignant nodules in the peritoneum; moreover, as I have myself observed in dogs, ligature of the portal vein does not produce ascites. The amount of ascitic fluid is very variable, and occasionally paracentesis is required. As the quantity increases the pain often lessens, and the observer may find it necessary to make a sudden deep depression in the abdominal parietes in order to feel the liver—to dip for it, as the phrase is.

Occasionally the growth extends through the diaphragm and sets up right-sided pleuritic effusion. The effused fluid is then usually blood-stained, and in quite exceptional cases an empyema may form. Even without pleural effusion, if the liver be very large, we find physical signs of compression of the lower part of the right lung. The weight of the liver may also hamper the circulation through the vena cava; if so, the *superficial abdominal veins will show up as prominent dark blue cords on the dark green wasted skin. Thrombosis may take place in either* internal saphena vein, and towards the end of the case a little albuminuria may appear. The spleen is very rarely enlarged. As in many other diseases of the liver, the urine may be loaded with lithates; and as in cancer of other organs, we occasionally meet with indicanuria, and in a few cases with slight pyrexia of a hectic type. Some patients suffer from an annoying reflex dry cough. When cancer is discovered in the liver a thorough search must be made for the primary seat.

Prognosis.—If the diagnosis is correct, death is inevitable. Usually all is over in less than six months. Some patients die very rapidly, even in a few weeks. I have recently had under my care a patient who only began to complain of weakness six weeks, and gave up work three weeks before death, yet he became rapidly jaundiced, and his liver weighed nineteen pounds. On the other hand, life may be prolonged for a year (and some authors say even longer) after the symptoms have declared themselves; it is a point of considerable importance that at any period the condition of the patient may remain stationary for weeks together, and under careful dieting and rest in bed even improve for a time. I once saw a clergyman in consultation in whom this respite occurred, and the friends, much to the annoyance of the medical attendant, persistently spread the report that the diagnosis must be incorrect. My experience of malignant disease certainly is that if after a thorough examination we have satisfied ourselves that the patient is suffering from it, we ought to hesitate very much before we surrender this diagnosis. I have known patients live over a year after a malignant growth in the stomach was palpable.

Diagnosis.—If this rest principally on the physical examination of the liver, many fallacies beset us. One is that the liver may appear irregularly enlarged when it is normal, and the apparent enlargement may be due to hardened fæces in the transverse colon, which is tender from the enteritis set up by them. Bright gives some excellent instances in point in his memoir on abdominal tumours. An enema will generally clear up this mistake. I have seen tumours of the stomach and also the thickened puckered omentum that is found in chronic peritonitis, whether simple, tubercular, or cancerous, considered to be the thickened indurated edge of a liver affected with cancer. A careful consideration of the shape of the tumour, the detection of the edge of the liver above it, and, in the case of an omental tumour, the discovery of resonance between it and the liver, together with a proper estimation of all the symptoms of the case, should prevent this error. I have also known a renal enlargement ascribed to the liver; and in all such cases the error has been largely due to forgetfulness of the fact that as the stomach, the kidney, and the colon to which the omentum is attached, touch the liver they may well, like the edge of it, make a considerable excursion during deep breathing. Then, again, tumours in the wall of the abdomen occasionally lead to mistakes, or the liver may appear enlarged when, in reality, its *size is unaltered. For example, it may be pressed down by lacing, by* pleural effusion, by pericardial effusion, or by an abscess between it and the diaphragm; or the line of hepatic dulness may be higher in the chest than normal, because the liver is pressed up by ascites or some large intra-abdominal tumour. Lastly, an enlargement of the liver may be concealed by tympanites or emphysema.

But even when we have evaded all these fallacies, our difficulties are by no means at an end. Often there is no easier diagnosis in medicine than that of cancer of the liver, but in those cases in which the primary growth cannot be found it may be very difficult, and if at the same time the liver is not enlarged, it may be almost impossible. Fortunately such a combination is rare, unless the cancerous deposit in the liver is limited to a few small nodules. In the only specimen of contracting carcinoma we have in the Museum at Guy's Hospital there was a primary growth in the breast. At the bedside the question nearly always takes this form.— Is this patient, who has no decided evidence of any primary malignant disease and whose liver is enlarged, suffering from malignant disease of it? The liver may not only be enlarged by malignant disease, but also from passive venous congestion, as in heart disease, passive portal congestion, the active congestion of hot countries, malaria, yellow fever, leuchæmia, Hodgkin's disease, pernicious anæmia, diabetes, fatty liver, hydatid, tropical abscess, the single large abscess of those who have never been abroad, suppurating hydatid, actinomycosis, tubercular abscess, obstruction of the common bile-duct, lardaceous disease, hypertrophic cirrhosis, congenital syphilis, and acquired syphilis, moreover, in perihepatitis, if the capsule be very thick, it may appear a little enlarged.

The majority of these diseases never present any difficulty, but the big cirrhotic liver, the syphilitic liver, and, much more rarely, obstruction of the common bile-duct, or hydatid, often give rise to much hesitation.

The large cirrhotic liver is uniformly large, and the palpable nodules on the surface of it are small. Sir William Jenner says that if any of them appear bigger than a cherry the case cannot be cirrhosis; they are never umbilicated, and neither they nor the whole liver ever tangibly increase in size in a few days; and although pain and tenderness may be present, neither of these is as severe as it usually is in cancer. Although jaundice is seen only in about half the cases of growth, and in about the same proportion of the cases of hypertrophic cirrhosis, yet this symptom is often the very means of establishing a diagnosis; for in hypertrophic cirrhosis the jaundice is not commonly very deep, and it always remains yellow; but in cancer it soon becomes intense, and slowly changes to the characteristic deep dirty green colour already described. A patient with malignant disease often dies soon after the occurrence of either jaundice or ascites, but he frequently lives many months; on the other hand, the supervention of these symptoms in the large cirrhotic liver usually points to death in less than ten weeks The obstruction to the flow of bile is never great enough in cirrhosis to cause distension of the gall-bladder or definitely clay-coloured stools, so that either of these symptoms would turn the scale in favour of malignant disease. The spleen is enlarged in rather more than half the cases of hypertrophic cirrhosis, and but rarely in malignant disease. Regard must, of course, be paid to the history and the age of the patient and to the lack of any other evidence of alcoholic poisoning. The aspect of the patient and the dryness of the skin may suggest cancer, but we must remember that wasting may be very marked in cirrhosis. Lastly, piles are more common in cirrhosis than in cancer.

The diagnosis between malignant disease and syphilis may be difficult. Congenital syphilis, although, if there be much fibrous tissue and gummas very numerous, it may cause the liver to be irregularly enlarged and hard, is probably never detected in this organ after puberty, because, I suppose, before then the gummas are all absorbed Acquired syphilis also leads to the formation in the liver of deposits of fibroid tissue and gummas. As the former contract and the latter are absorbed, scar-like depressions mark the surface, and between them the unaltered liver substance, which has undergone compensatory hypertrophy, projects, and these nodules of healthy liver and those of unabsorbed gummas cause the liver to be covered with lumps of all sizes, giving the whole organ on physical examination a close resemblance to a cancerous liver; this is the more embarrassing as, owing to syphilitic lardaceous disease of it, the total enlargement may be quite as great as is usually the case in hepatic cancer. It is conceivable that the glands in the transverse fissure might be much enlarged from gummatous deposit —and we have a specimen in Guy's Hospital Museum showing this; if so, they might press on the common bile-duct and cause jaundice and distension of the gall-bladder, but this and the deposition of lardaceous material in them are pathological curiosities· if, then, the patient be jaundiced, or his gall-bladder distended, it is all but certain that the enlargement of his liver is not syphilitic. It is, too, within the range of possibility that in the same patient syphilis might not only distort the liver, but also cause perihepatitis and chronic peritonitis, and so induce ascites; however, not only is it extremely unlikely that two rare results of syphilis should be present in the same case, but the perihepatitis would smooth over the syphilitic irregularities on the liver. In a case of doubt, therefore, ascites is very strong evidence in favour of cancer. Other points of distinction are that we never find in syphilis the rapid enlargement of the whole liver or its nodules that may occur in cancer; on the other hand, in cancer we never get the marked diminution of both that we find in syphilis, especially in cases under treatment by iodide of potassium. Pain and tenderness are not so extreme in syphilis as in cancer. Rapidity and great severity of the general symptoms are, of course, much in favour of cancer; and I need hardly add that a careful search must be made for other signs of syphilis.

Cases in which, owing to non-malignant obstruction of the duct, bile is retained in the liver, causing it to be enlarged and the patient to be jaundiced, sometimes present very great difficulty. Nearly always gall stones have set up chronic inflammatory thickening outside the common and cystic ducts. A remarkable instance is recorded by Bright, in which the parts about the entrance of the common duct into the duodenum were thus hardened and matted together. The common, hepatic, and cystic ducts were dilated to the size of a healthy gall-bladder, and the gall-bladder was so dilated that, both during life and after death, it almost reached the crest of the ilium. The ducts in the liver were dilated into a number of vesicles. The pancreatic duct was also much dilated. The patient, a woman aged fifty-six, gave a history of spasmodic pains five years before admission. She was jaundiced and had great hepatic pain and pale stools for four and a half months before she died drowsy from cholæmia. She was very sick and wasted much, but the jaundice was never of an olive green colour; in fact, it was stated to be brilliant a few days before her death I have recently seen, with Mr. A. G. Wells, a lady aged about sixty who had suffered from gall-stones years before. Her present illness consisted, on our visit, of some loss of flesh, much hepatic pain and tenderness, enlargement of the liver, jaundice, vomiting, constipation, and white stools. Here the diagnosis lay between growth and inflammatory thickening. A fortnight before death the jaundice disappeared, but a day or two afterwards symptoms of pyæmia set in. At the post-mortem examination we found so much inflammatory thickening on the under surface of the liver that it took some time to discover the gall-bladder; this was empty, sloughing, and contained a gall-stone. The common and hepatic ducts were enormously dilated, and in the former lay a gall-stone easily movable; and no doubt the accidental shifting of it led to the disappearance of the jaundice. The liver was studded with minute abscesses. To show how extensive this inflammatory thickening due to gall-stones can become, I may mention that I once made a post-mortem examination on a woman who during life had had almost complete pyloric obstruction. This was found to be due to inflammatory thickening and matting which started from the gall-bladder and invaded the pylorus. It was set up by numerous gall-stones.

The main points of distinction between cancer of the liver and inflammatory thickening about the biliary passages are that in the latter case the patient does not look as though she were suffering from cancer; the hepatic enlargement is uniform, never so great as it often is in cancer, and the jaundice does not become dark green. If it disappear for a time, this probably means that a gall-stone has shifted its position; that the jaundice of cancer should disappear is almost unknown.

Hydatid of the liver seldom gives rise to difficulty, for usually the tumours are only one or two, and they are smooth, regular, not tender, cause neither pain, jaundice, ascites, nor general emaciation, and may give a thrill. It is extremely rare for a hydatid tumour to press on a bile-duct and so lead to jaundice, which is, however, occasionally caused by the rupture of a hydatid cyst into the bile-duct. Such a case may be extremely difficult to diagnose, but our chief guides will be the sudden onset of jaundice, the physical examination of the liver, and the absence of wasting and pain. The exogenous form of hydatid may form multiple tumours, and these and the multiple tumours formed by the alveolar or, as it is often called, multilocular variety, may, if they happen to cause jaundice, give rise to great uncertainty. But they are so rare that it will be necessary to think of them only in those instances in which the age, the wasting, and the long duration of the illness lead to the conclusion that the case cannot be one of cancer.

Treatment. This can only be palliative. Morphia may be given to relieve the pain, and sometimes the pruritus is so intractable that it yields to nothing else This symptom is often most distressing Perhaps pilocarpine subcutaneously or warm alkaline baths are the best remedies Constipation and vomiting will be treated on ordinary principles, for the latter it is often of great service to wash out the stomach The ascites may require paracentesis. Quite recently Mr. Mayo Robson has described a case in which he excised a cancer of the liver, but suitable cases must be excessively rare.

PRIMARY CANCER OF THE LIVER—There is little doubt that many cases formerly regarded as instances of primary carcinoma of the liver were examples of secondary deposit in that organ, and I have therefore examined our recent records at Guy's Hospital, and shall only use for the basis of this description cases in which a careful autopsy showed that the growth was undoubtedly primary in the liver: I have excluded all in which there was a deposit in any other organ, except that in one or two a minute nodule was detected in the lung.

During the twenty-four years, 1870-1893, both inclusive, eleven such cases have been seen in the post-mortem room, and about 11,500 post-mortem examinations have been made. Therefore, less than 0·1 per cent of all the persons who die in a large hospital succumb to primary carcinoma of the liver The proportion of undoubted primary to secondary carcinoma of the liver is about 1 to 25. During these twenty-four years there have been seven cases in which the growth was by some regarded as primary in the liver, although many other organs were affected; but, inasmuch as the primary seat of these cases must to some extent be a matter of conjecture, they have not been used as a basis for this account. Frerichs gives the proportion of primary malignant disease of the liver (without growth elsewhere) to other cases of malignant disease of the liver as 1 to 5; but the post-mortem examinations of all his cases were made prior to 1861, and I think it probable that improved systematic methods of careful search for the primary seat, and the fact that Frerichs does not allude to the possibility of the primary seat being in the gall-bladder or bile-ducts, will explain the difference between a proportion of 1 to 5 and 1 to 25.

There are three forms of primary cancer of the liver In the most common form the new growth is deposited in nodules, and the whole liver exactly resembles the organ when it is the seat of secondary deposits Out of the eleven cases from Guy's Hospital six fall into this group.

In another form the growth consists of one large tumour in the liver. A very good instance in point is recorded by Bright in his memoirs on abdominal tumours. Here "the tumour within the liver was the size of an adult's head and of rounded form." It was in the left lobe of the liver, and many of the recorded cases have begun there Schueppel states that such a growth may destroy half the liver, that caseous degeneration and hæmorrhages in it are common, but that the portal glands are not often enlarged. Among the eleven cases from Guy's there is none in which there was a single large tumour, but there were two in which one cancerous mass was huge, and the rest were quite small, so that these cases perhaps belong more to this group than to the first.

In the third group the cancer cells are uniformly diffused through the liver, and there is a great increase of fibrous tissue in all directions. This often contracts, so that, although at first the liver is larger than normal, later it may be smaller Three out of the eleven Guy's cases were considered by Dr Fagge (4) to belong to this group, and the livers weighed respectively 180, 62, and 36½ oz. In these cases the organ is very hard, retains its shape, and looks like a coarse cirrhosis, the nodules varying in size from a pea to a cherry. When cut it also resembles cirrhosis, for there are wide, white, vascular bands of connective tissue running through the organ, the gland tissue between them has vanished, and, according to Schueppel, in an extreme case, every hepatic acinus has been replaced by one of cancer On scraping, some white fluid may be obtained, but Schueppel states that the retrogressive changes hardly ever go farther than fatty degeneration of the cells, and hæmorrhage is never seen, but in two of the three cases recorded by Dr Fagge some of the cancerous masses were cheesy and would shell out, and in one case there was hæmorrhage into them. The glands in the portal fissure are rarely affected, the cancer hardly ever grows into the bile-ducts, and only rarely into the portal vein, but it has been described as implicating the gall-bladder. Secondary growths in other parts of the body are almost unknown. We see, therefore, that this form of cancer differs much from the common variety; and this, together with the naked eye and microscopical resemblance to cirrhosis, accounts for the fact that some observers often regard a case as cirrhosis which others regard as primary infiltrated carcinoma.

The following analysis of the chief points of the eleven cases we have had at Guy's Hospital brings out the leading features of primary cancer of the liver:—

Age.—The case of a boy aged twelve, recorded by Dr. Pye Smith (7), had better be omitted from consideration here, because, judging by his ex-

treme youth and the exceptionally long duration of the disease, it is probable that his case was one of some extremely rare affection of the liver of which we know little. In the remaining ten cases the oldest patient was seventy-one years old, and the youngest twenty-three. Five were more than fifty years old. Of seven cases (which, as sarcoma is so rare, we may assume to have been mostly cancers) recorded in the Pathological Society's *Transactions* from 1871 to 1891 in sufficient detail to be available, and not included in the eleven cases from Guy's Hospital, the oldest patient was sixty-nine years, and the youngest thirty-three, five were over fifty. We thus see that it is a disease of adult life, and generally of old age—a fact which is equally true of secondary cancer of the liver.

Sex.—Among the eleven Guy's Hospital cases, six were men and five were women; and among the seven cases of the Pathological Society two were women and five were men; so that among eighteen cases eleven were men. This is interesting, as confirming the assumption that these were genuine cases of primary malignant disease of the liver; for we have seen that secondary hepatic cancer is commoner in women than men.

Family history.—In none of the clinical reports of these eleven cases is it said that any of the patients' relatives had cancer. It is very difficult to obtain an accurate family history from hospital patients; but as there was no family history of cancer in any of the cases of primary malignant disease of the liver recorded by Murchison, the point is worthy of further investigation.

Symptoms.—As might be expected, the patients are often wasted, sometimes they vomit; often there is constipation, but the stools are never mentioned as being pale. If the jaundice be sufficient, a little bile may be detected in the urine, which in two instances contained albumin.

Temperature.—In four cases the temperature ranged about 101° or 102°; in one, in spite of extreme collapse, it was 99°, and Murchison gives two cases of primary malignant disease with pyrexia; it appears, therefore, to be commoner when the disease is primary in the liver than when it is secondary. If this should turn out to be the case, it may be of some value as a means of diagnosis.

Jaundice.—Out of the eleven Guy's cases, in five there was no jaundice, in two it did not appear till just before death, in three it was slight, and in one it was considerable. Among the seven cases of the Pathological Society it is only mentioned as being present in four, and in one of these it was slight. We may thus conclude that in primary malignant disease of the liver jaundice may be absent all through the illness; if present it is usually slight, and comes on late. We never meet with the long-lasting dark staining so common when the liver is affected secondarily. The explanation of this may be that, as the disease is rapidly fatal, there is not time for jaundice to supervene. It cannot be entirely due to the circumstance that the portal glands are rarely enlarged in primary carcinoma of the liver, for in the only case in which the jaundice was deep it is expressly stated that the portal glands were normal. Probably the *rarity of their enlargement is due to the death of the patient before there* is time for infection of them to take place.

Ascites.—In seven of the eleven Guy's Hospital cases there was ascites, and in most of these it was sufficient to be detected during life. Among the seven cases of the Pathological Society ascites is only definitely mentioned as being present during life in two; and in one other a little fluid was found at death. Probably we shall be near the mark if we say that in about a third of the cases there is definite ascites capable of detection during life. The growth often grew into and caused thrombosis of the branches of the portal vein, and in some cases this may explain the ascites.

Enlargement of Liver.—The liver, which was usually painful and tender, was always enlarged except in the instance in which it only weighed 36½ oz. I found that among fifteen cases of primary malignant disease of the liver which are available, in the Guy's Hospital and the Pathological Society's cases, for calculating the weight, the heaviest was 267 oz., the next 200 oz., and the least 36½ oz. The one of 200 oz. was the exceptional case in the boy aged twelve, and the one weighing 267 oz. is recorded as a case of sarcoma. If we exclude these two the average is 116 oz., or if we only exclude the boy it is 127 oz. The usual weight is from 120 to 130 oz.

Prognosis.—Omitting, for the reasons already given, the case of the child, I find that, after the first symptom appeared, two patients lived four months, three lived three months, one lived two and a half months, two lived two months, and in one the duration could not be determined. That gives, roughly speaking, an average duration of twelve weeks. It is especially noteworthy that there are no wide limits of duration, so that it may be safely said that primary malignant disease of the liver is usually rapidly fatal; thus forming a striking contrast to those cases in which the organ is affected secondarily, and in which the patient often lingers for a long while. This conclusion is fully borne out by the cases recorded in the Pathological Society's *Transactions*, for in the four in which it is mentioned the duration was two, a half, three, and two months respectively.

It appears, therefore, that primary cancer of the liver resembles the secondary form in many symptoms, but that the duration from the first symptom probably never exceeds four months. Less important facts are that it is probably commoner in men than in women, pyrexia is not infrequent, jaundice is never deep olive green, is often absent, and if present is usually slight, and the motions are rarely pale. The glands in the portal fissure are not often enlarged.

In one case treated at Guy's Hospital disease of the liver was never suspected. A woman aged thirty-nine was admitted for what was regarded as the vomiting of pregnancy; there was no jaundice, and no one even thought of disease of the liver. Premature labour was induced, but the woman sank. The post-mortem revealed the fact that the liver was the seat of extensive malignant growth, but that all the other organs of the body were absolutely normal. A case almost parallel to this is recorded by Tivy, in which, if the abdomen had not been examined and the liver found to be enlarged, it would have been impossible during life to suspect disease of this organ; yet the man *quickly sank and died. To be quite accurate, I ought not to have used* the cases recorded, in the Pathological Society's *Transactions,* as sarcoma, but I have done so because primary sarcoma is very rare, and is clinically indistinguishable from cancer. Frequently, moreover, there is much variance of opinion among histologists whether a primary growth be a carcinoma or a sarcoma, but all the eleven cases in Guy's Hospital were regarded as carcinoma.

Perhaps this is the most suitable opportunity to call attention to the fact that malignant disease occurs occasionally in a liver which is cirrhotic. This happened in the last of the cases of primary malignant disease of the liver which occurred at Guy's Hospital. The patient, a man aged forty-nine, had drunk hard, and he was admitted under Dr. Goodhart in 1892 for ascites and right pleural effusion. When the ascitic fluid was drawn off, a lump was felt in the hepatic region, he was never jaundiced, and he died three days after the paracentesis. The liver weighed 118 oz., and there was extreme cirrhosis in the parts unaffected by the growth, which formed a large mass in the right lobe together with smaller masses scattered about in the rest of the liver. It was a spheroidal carcinoma. Our museum contains the liver of this case, and also that of a man aged sixty-eight, who was under Dr. Pye-Smith in 1891, and in whom at death a spheroidal carcinoma was found in a cirrhosed liver. In 1885 I made a post-mortem examination on a man aged sixty-three, also under Dr. Goodhart. He had sarcoma of many bones. There was a secondary growth in the liver which weighed 60 oz. and was very hard and cirrhosed.

PRIMARY CARCINOMA OF THE GALL-BLADDER.—This is not nearly so rare as was formerly supposed. Most authors agree that often it owes its origin to gall-stones, which are present in 95 per cent of the cases, and this explains the fact that it is four times as common in women as in men. Secondary deposits in the liver and in the glands in the portal fissure are very common, and therefore the symptoms are much the same as those of secondary carcinoma of the liver, except that in 68 per cent of the cases a definite tumour can be felt in the region of the gall-bladder, and frequently there is a history of gall-stone colic. Carcinoma of the gall-bladder often spreads by extension to the liver, stomach, and colon. An excellent account of the record of the subject is given by Ames (1).

PRIMARY CARCINOMA OF THE BILE-DUCTS.—Our knowledge on this subject has been recently put together by Dr. Rolleston (9). The growth is nearly always a cylindrical-celled carcinoma; and when it takes place in the bile-ducts within the liver it is, until examined histologically, very liable to be confounded with primary carcinoma of the liver. When the growth occurs in ducts outside the liver it thickens their walls and fills their lumen with shaggy growth. The gall-bladder and the ducts behind the growth become very much distended. It is about equally common in men and women. The chief symptoms are deep jaundice, pain, and uniform enlargement of the liver. *Usually the organ contains but few secondary* nodules, and therefore they are not felt during life. It is obvious that it is in these cases that cholecystenterostomy is most likely to afford temporary relief.

SARCOMA OF THE LIVER.—This occurs in two forms, primary and secondary. As has just been mentioned, the primary cannot be distinguished, clinically, from carcinoma, and after death it often happens that it is a very difficult matter to decide between them. I have known different opinions given upon the same section. Its extreme rarity is evident from the fact that none of the eleven cases of primary malignant disease which I have quoted as found in the post-mortem room at Guy's Hospital were sarcomatous. A primary sarcoma of the liver, which weighed nearly 17 lbs., is recorded in the Pathological Society's *Transactions*.

Secondary sarcomas in the liver exactly reproduce the form of the original growth. They are rarely diagnosed, for the patient usually dies before they give rise to symptoms. In the years 1885-93 we have had six cases at Guy's Hospital. The primary seat was in the bones in five cases; the secondary growths were usually very numerous in various parts of the body. In most of the cases there was a solitary growth in the liver, and in one this was 2½ inches in diameter. In one only were the secondary growths very numerous, and then they were small.

PIGMENT TUMOURS OF THE LIVER.—These tumours, which are either sarcoma or carcinoma, form such striking objects that museums contain many specimens. They only differ from the sarcomas and carcinomas, already described, in that the growth is coloured black or dark brown; and under the microscope the cells of the tumours are seen to be of a brown colour, and many contain abundant black pigment granules. Melanotic sarcoma is much more common than melanotic carcinoma, and these sarcomas are almost always secondary to a melanotic sarcoma either in the eye or the skin. Many cases are on record: for instance, Bright gives two, in both of which, from the presence of melanotic deposits in the skin, a correct diagnosis was made. In both the liver was enormous. The second case illustrated the usual form, for there were innumerable melanotic nodular tumours in the liver. In the first case the melanotic new growth was diffused uniformly throughout the liver. This diffuse melanosis is very rare, but is mentioned by Schueppel. In Bright's case some non-melanotic secondary tumours were associated with this diffuse melanosis; and sometimes in the same case we find some of the secondary nodules pigmented while others are free. Often only one or two melanotic sarcomatous masses are found in the liver; doubtless because the patient died before others could form. We have a specimen in Guy's Museum in which there was only one tumour. Sometimes, as in Dr. Murchison's case, although numerous, they are so small that they produce no symptoms.

There are at least five cases of primary melanotic sarcoma of the liver on record: one by Frerichs, one by Block, one by Delépine, one by Wickham Legg, and one by Holsti (5). Block records his as an example of endothelioma, but Schueppel thinks there is no doubt that it was sarcomatous.

Melanotic carcinoma is excessively rare. I have, however, seen one case. The only symptoms observed during life were progressive wasting and uniform hepatic enlargement. The liver weighed 122½ oz. I made the post-mortem examination, and there is no doubt the growth was primary in the liver. The case is described in full (14). In Delépine's case the tumour grew so rapidly that the patient positively gained weight (3).

Pigmentary malignant disease has no separate clinical symptoms from ordinary malignant disease; so unless a primary melanotic tumour is discovered during life it cannot be foretold that pigment will be found in the hepatic growths, unless, on exposing the urine of such a patient to the air, a brownish or blackish discoloration of it were to appear (melanuria), when a tolerably sure indication of the kind of growth would be obtained.

ADENOMA.—There is often considerable variety of opinion among histologists as to the exact boundary-line between adenoma and carcinoma of the liver; in fact, some regard adenoma as merely a stepping-stone to carcinoma. It would be well, as Coats suggests, to limit the word to the form known as nodular hyperplasia; for the other so-called adenomas—as, for example, Greenfield's case (11)—have more the habit of cancer. Restricting the name in this way, we may describe adenomas as perfectly well-defined tumours having the same structure as proper hepatic tissue, except that the cells are a little larger than is usual, and often have double nuclei, and there may be an increase of fibrous tissue between them. If large, the tumours are solitary, and we have a specimen in our museum in which a globular mass 1¼ inch in diameter protruded from the surface of the liver. It consists, histologically, of normal liver tissue, except that there is an excess of fibrous tissue. The patient was twenty-six years old; he died of strangulated hernia. If the tumours are small, they are multiple and sharply defined. They are rare in man, but common in dogs. Sometimes an excess of fibrous tissue surrounds them. These innocent adenomas never give rise to symptoms during life.

Lymphadenoma.—New formations consisting of lymphoid tissue, either generally diffused through the liver or occurring as nodules, are not uncommon; but they are only met with in Hodgkin's disease or in leuchæmia, and then form but a part of a widespread formation of lymphoid tissue.

Cavernous angioma of the liver is common, but produces no symptoms during life. Murchison refers to a case of myxoma and to one of cystosarcoma, but these are too rare to be of any clinical interest. Cysts of the liver, not hydatid, are so exceptional, so infrequently give rise to any symptoms during life, and are so obscure in their mode of origin, that the discussion of them would be out of place here. They are very fully considered in the following papers, in which also references on the subject will be found (8, 10, 11, 13). Minute fibromas are occasionally found in the liver in the post-mortem room, but they do not cause any symptoms.

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REFERENCES

1 AMES. *Johns Hopkins Hospital Bulletin*, v. No. 41.—2. BLOCK. *Arch. d. Heilk.* xiv. 1875, S. 412.—3. DELÉPINE. *Trans. Path. Soc. Lond.* xlii. p. 161.—4. FAGGE. *Path. Trans.* vol. xxxi. p. 125.—5. HOLSTI. *Brit. Med Jour. Epit.* May 25, 1895.—6. LEGG, WICKHAM. *St. Barth. Hosp. Rep.* xiii. p. 160.—7. PYE-SMITH. *Path. Trans* xxxi. p. 125.—8. *Ibid.* xxxii. p. 112.—9 ROLLESTON. *Med. Chron.* Jan. 1896.—10. SAVAGE and HALE WHITE. *Path. Trans* xxxiv. p. 1.—11. SHARKEY. *Path. Trans.* xxxiii. p. 168.—12. TIVY. *Path. Trans* vol xxv.—13. HALE WHITE. *Path. Trans.* xxxv. p. 217.—14. *Ibid.* vol. xxxvii. p 272

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DISEASES OF THE GALL-BLADDER AND BILE-DUCTS

INTRODUCTORY AND GENERAL REMARKS.—Until quite recently diseases of the gall-bladder and bile-ducts could be adequately considered with diseases of the liver; but the general advance of medicine, and its closer alliance with surgery, have given to these affections a place of their own in medical literature.

Before the last decade the ailments in question were studied from a purely medical standpoint—the standpoint still in the earlier stages of all cases, and throughout the entire course of many; but in no cases have the recent advances in surgery brought about such an enlargement of our resources, nor in any have the physician and surgeon been able to combine their forces to better effect. Yet even now we must not feel altogether satisfied; much still remains to be done in this field of work, not only from the pathological point of view and in the perfecting of diagnosis, but also in effecting a more scientific and direct therapeusis, in perfecting the older methods, and possibly in inventing more complete and thorough surgical procedures.

I propose to consider the subject under three heads:—(i.) Inflammatory affections of the gall-bladder and bile-ducts; (ii.) Tumours; (iii.) Gall-stones.

INFLAMMATORY AFFECTIONS OF THE GALL-BLADDER AND BILE-DUCTS.—These may conveniently be considered under the following divisions·—A. Catarrhal inflammations: (*a*) Acute catarrh (Catarrhal jaundice), (*b*) *Chronic catarrh*. B. Suppurative inflammations: (*a*) Suppurative *catarrh*: (*α*) *Simple empyema*, (*β*) *Suppurative cholangitis*; (*b*) Ulceration, perforation and stricture of the gall-bladder and bile-ducts; (*c*) Acute parenchymatous inflammation and gangrene of the gall-bladder.

Catarrh of the gall-bladder and bile-ducts.—The larger bile-ducts and the gall-bladder, being lined with mucous membrane having a cylindrical epithelium and ordinary racemose glands, like other mucous passages, are subject to catarrh which may be acute or chronic.

Acute catarrh is supposed to give rise to that evanescent form of icterus, known as catarrhal jaundice, which more frequently occurs in young persons, usually comes on as a sequence of dyspepsia or as a result of exposure to cold, and is ordinarily unaccompanied by pain or serious illness; medical help is sought on account of the marked objective symptom of jaundice.

When it is borne in mind that the bile-ducts have a small calibre, that the mucous lining is capable of swelling, and that the secretion of bile takes place under very low pressure, it is easy to suppose that catarrh in this situation may lead to jaundice, though absolute proof of this causation is wanting; simple catarrhal jaundice furnishes no necropsies. Fagge, indeed, doubted that catarrh of the bile-ducts gives rise to swelling of the mucous membrane. He says: "A more probable suggestion is that catarrh of the duodenum obstructs the oblique and narrow passage of the duct through the walls of the gut." If so, we may ask why jaundice does not more commonly follow what is probably a frequent disorder. Moreover, we should expect a chronic catarrh to produce permanent jaundice.

The usual cause of acute catarrhal jaundice is probably an extension of inflammation from the duodenum; and as the common bile-duct traverses the walls of the duodenum very obliquely, this narrow terminal portion of the duct is usually the seat of the primary obstruction. Beside gastro-intestinal catarrh, exposure to cold, extension to the bile-ducts of inflammation from the parenchyma of the liver, carcinoma of the liver, gall-stones, hydatids, pneumonia, and other acute inflammations and infectious fevers must be mentioned as causes of catarrh, direct or indirect. Murchison gives gout and syphilis as causes, and under this head Fagge includes jaundice due to fright and that occurring in epidemics. Although it is well known that in cancer of the liver jaundice is a very variable sign, it is not always recognised that the icterus is at times dependent on an associated catarrh which may be relieved by treatment, though the original disease persists and progresses. The same remarks apply with almost equal force to multilocular hydatids.

The symptoms of acute catarrh of the bile-ducts (catarrhal jaundice) may be so slight that the patient may know nothing of his condition until he is told that he is yellow; but ordinarily symptoms of gastro-intestinal disturbances—such as coated tongue, bad taste, eructations, want of appetite, nausea and sickness—precede the jaundice. According to the duration of the jaundice so will be the interference with health *and with the general nutrition of the patient.*

Enlargement of the liver or of the gall-bladder is not seen in ordinary slight cases; but, if the affection be prolonged, the liver may be swollen and the gall-bladder somewhat enlarged. Under ordinary circumstances the symptoms pass off in two to six weeks, and the patient may feel quite well some time before the jaundice has quite disappeared.

In other cases, especially if carelessly treated, the disease may drag on for weeks or months, the liver enlarging and considerable emaciation taking place, so that the question of serious organic disease has to be considered.

Where, however, the symptoms depend on simple catarrh, recovery usually takes place under proper management; but if the acute catarrh complicates some other disease, the symptoms will depend on the cause, and may be both serious and persistent.

Though other symptoms may be almost absent, catarrhal jaundice always demands the most careful consideration, lest the case turn out to be one of acute atrophy of the liver; which, however, is fortunately an extremely rare disease. The absence of serious symptoms (especially of delirium and rapid pulse) and the usually speedy recovery under treatment are, as a rule, sufficient to enable a diagnosis to be made; but, as Dr. Donkin pointed out in reporting a case of malignant jaundice in a child two years of age, "a practical lesson to be learned from such cases is to be very guarded in the prognosis of all so-called and apparent cases of 'simple' or 'congestive' or 'catarrhal' jaundice in children, when the jaundice does not abate within a week, and still more when it increases" (11). The absence of pain and of the preceding characteristic gall-stone attacks will ordinarily distinguish simple catarrh from that accompanying cholelithiasis. Moreover, the jaundice in gall-stones usually passes off rapidly, or, if persistent, is generally intensified after pain, and is often associated with ague-like seizures. In cancer, catarrh of the bile-ducts is probably the chief cause of the jaundice; but loss of flesh, ascites, and nodules or tumour of the liver usually afford sufficient data for diagnosis.

In cirrhosis, the slighter degree of jaundice, the usually more advanced age, the previous history of drunken habits, and the ascites, together with the generally more serious symptoms and the physical examination of the liver, afford in nearly all cases sufficient help to prevent mistakes. As a rule it may be said that jaundice in a young person coming on without pain, or any apparent cause except disordered digestion, is most probably catarrhal.

As catarrh of the bile-ducts is generally an extension of duodenal catarrh, abstinence from alcohol, a light simple diet, and mild saline aperients are indicated. If other medicine be thought necessary, a simple rhubarb and soda mixture will answer well. Half a pint, or a pint, of the natural Carlsbad water, taken warm the first thing in the morning, is often of service as an aperient; if this be insufficient, a teaspoonful of Carlsbad salts can be added, or these salts may be taken in plain hot water. As a rule the patient need not be put to bed, but he should be warmly clothed and avoid chills.

If the cause be chill, a warm bath with hot applications over the liver and a diaphoretic medicine will be advisable. Salicylate of soda is said to be of service. As in jaundice the bile is principally excreted by the kidneys, it is important to maintain their action by diluent drinks and by other diuretics if required.

When the jaundice is long continued, the administration of oxgall may assist the assimilation of fats; and creasote may prove of service as an intestinal antiseptic.

Rectal injections of hot water, from one to two pints daily, at a temperature of from 60° to 90°, to be retained as long as possible, are said to prove beneficial by causing a contraction of the gall-bladder which may overcome obstruction due to accumulation of mucus in the common duct.

Chronic catarrh of the gall-bladder without jaundice forms a distinct and definite disease; and I have seen several cases in which careful observers had diagnosed cholelithiasis and had recommended operation, but in which neither the gall-bladder nor ducts contained anything firmer than thick ropy mucus, which seemed to be the cause of the painful contractions of the gall-bladder simulating gall-stone colic. In one case of this kind, in a lady of fifty-six on whom I operated, the gall-bladder contained bile mixed with thick mucus which formed plugs something like small grains of boiled sago There were no other signs of disease, but the gall-bladder was very large and pouched and its mucous membrane thickened. The gall-bladder was drained, and it was kept open for a fortnight; the wound was then allowed to close. The patient continues well, and is freed from her formerly frequent attacks.

Although in these cases the gall-bladder is usually distended it rarely forms a distinct tumour, and there is an absence of pain on pressure over it. Unless gall-stones have been present at some time there are usually no adhesions of the gall-bladder or ducts to the neighbouring viscera. This proves that the inflammation has not penetrated to the peritoneal coat, as usually it does when dependent on gall-stones.

This catarrh may be the sequence of gall-stone irritation; but in other cases it is probably due to the dependent position of the fundus of the gall-bladder, or to chronic constipation and accumulation of fæces in the hepatic flexure of the colon interfering with the regular emptying of the gall-bladder.

The diagnosis of this affection from cholelithiasis may usually be made by observing that the attacks are less severe and less prolonged than in gall-stone colic; that no gall-stones are found in the evacuations after an attack; that jaundice seldom supervenes, or if it do is only very slight; that there is no tenderness on pressure between the ninth costal cartilage and the umbilicus, and that the affection, as a rule, will yield completely to treatment. Should medical treatment fail to give relief, it may be difficult to distinguish chronic catarrh of the gall-bladder from cholelithiasis; but if, under the belief that the case is one of gall-stones, the gall-bladder be exposed and no concretions found, drainage of the gall-bladder will probably effect a cure.

Chronic catarrh of the bile-ducts may be simply a sequel of the acute form; it may then give rise to a more or less persistent jaundice leading to a suspicion of more serious organic disease. Although dyspeptic symptoms are present, due to the associated gastro-intestinal catarrh and jaundice, and some loss of weight, yet the retention of bodily strength, and the absence of such serious sequels as ascites, hæmorrhages, and so forth, generally suggest a good prognosis; moreover, the symptoms usually yield to proper treatment.

Catarrh of the bile-ducts probably always accompanies jaundice from whatever cause; and, as Dr. Moxon has pointed out, when an obstruction in the common duct is complete, a colourless mucus is always found in the bile-duct. A search through the pathological records of Guy's Hospital for twenty years failed to discover any exception to this rule. When the obstruction is partial the mucus may be charged with bile, as the backward pressure is not sufficient to stop the secretion and the pouring out of bile into the ducts.

As a concomitant of cancer of the liver and of the bile-ducts chronic catarrh is common, and is frequently the cause of the accompanying icterus. Thus the relief to the jaundice afforded by treatment in a necessarily fatal disease is accounted for; whereas when the jaundice is dependent on pressure of the growths on the ducts, it will be slightly or not at all influenced by remedies.

The same remarks apply to the effects of hydatids, of abscess, and of other organic diseases of the liver.

Gall-stones are probably always accompanied by catarrh and by the formation of thick, ropy mucus which, as it passes, sets up attacks of pain; and it seems not unlikely that some minor seizures of pain, followed by little or no jaundice, are of this nature—in which case, of course, no gall-stones will be found in the evacuations.

Chronic catarrhal jaundice needs practically the same treatment as the acute form: careful dieting, regular exercise, a saline aperient in the morning, and an alkaline medicine, being the chief means required. In case the disease prove obstinate, treatment at Carlsbad or Harrogate will probably be of service.

Should the catarrh depend on organic disease, the treatment may require some modification to meet the special features of the case.

In chronic catarrh of the gall-bladder, regular exercise, massage over the hepatic region, the avoidance of anything tight round the waist (which will increase the dependence of the fundus of the gall-bladder), careful regulation of the diet, and the judicious employment of saline aperients, should in all cases be recommended.

A tumblerful of the natural Carlsbad water, with a little hot water, *taken before breakfast each morning; and every other morning, in addition, a dose of Carlsbad salts, or of sulphate of magnesia,* are undoubtedly useful; as is also an alkaline tonic dose containing soda and nux vomica taken before lunch and dinner.

The spasmodic attacks may require the administration of a sedative if slight, a grain of exalgine in hot water, repeated in half an hour, will often relieve the pain; or twenty drops of spirit of ether in half an ounce of chloroform water, the dose to be repeated every fifteen minutes until relief is obtained. The application of hot fomentations, and the administration internally of a pint of hot water, will at times afford efficient relief; but in some cases nothing short of a subcutaneous injection of morphia will suffice. If, after a few weeks of general treatment, the symptoms are not relieved, the disorder will probably be attributed to gall-stones, and operative treatment will be considered If the gall-bladder and ducts be found free from gall-stones, cholecystotomy and drainage should nevertheless be performed; and it will be found useful after the third day to syringe a little warm water gently through the drainage-tube daily so as to wash out the ducts; after a week or ten days the tube may be left out, and the wound allowed to close.

General treatment directed to the causes should be continued for some time afterwards.

Suppurative inflammation of the bile passages.—At first sight suppurative inflammation of the gall-bladder and bile-ducts would seem to be capable of description in small compass and under one heading, but the subject is by no means as simple as it would appear.

For instance, simple empyema or suppurative catarrh of the gall-bladder, which is closely allied to suppurative cholangitis, differs altogether from phlegmonous cholecystitis; this latter, however, is also associated with pus in the gall-bladder, and may thus quite properly be called an empyema. Phlegmonous cholecystitis, however, if not operated on expeditiously, is one of the most fatal of diseases, as not only is there a tendency to gangrene, but also to a rapidly-spreading and lethal form of peritonitis. The different clinical characters of suppurative inflammation can probably be accounted for by the presence or absence of certain organisms; and although the bacteriology of this region is still in its infancy, sufficient good work has been done to make a review of it well worth our consideration. It has been supposed that the bile is an antiseptic fluid which tends to prevent decomposition in the alimentary canal; but in a series of observations which I published some years ago on a case of biliary fistula (31), I found that the absence of bile from the intestine of a woman during a period of fifteen months did not lead to any irregular fermentative process; the alleged antiseptic effect of bile on the fæces is, therefore, probably imaginary. Normal bile is, however, generally sterile: this was proved by Netter in 1884, who experimented on dogs; and the fact has been confirmed by Gilbert and Girode, and, later, by Naunyn, who found it sterile in two cases *within a few hours of death.*

In a case of mucous fistula, due to stricture of the cystic duct, the constantly clean appearance of the edges of the fistula suggested to me that the fluid secreted by the gall-bladder might possess antiseptic properties; moreover, when collecting the fluid for experimental purposes, I found I could leave the flasks exposed to the air for several days without any apparent change, an observation which strengthened the presumption. Professor Birch, to whom I supplied some of this fluid, performed numerous cultivation experiments, and came to the conclusion that its antiseptic properties were but slight, the want of change being probably due to poverty of the fluid in nutrient materials (3).

When, however, the flow of bile from the cystic duct is arrested, micro-organisms often enter the gall-bladder; and Charcot and Gombault, after ligaturing the common duct in dogs, demonstrated the presence of organisms within the gall-bladder.

This observation was confirmed by Netter, who found that twenty-four hours after aseptic ligature of the common duct in dogs, organisms—a staphylococcus and B. coli communis—could be cultivated from the bile.

The B. coli communis is said to be the most abundant and most frequent of the bacteria found in the healthy man. It has been demonstrated in every part of the alimentary canal, from the mouth to the anus. It varies greatly in its virulence, and in experiments on animals it appears to be harmless when taken from the normal intestines. If, however, the intestine, or its diverticula, become the seat of a morbid process, then the bacillus becomes virulent. At one time, as shown by Escherich, it may act as an ordinary pyogenetic organism producing local abscesses; at another as an active pathogenetic organism producing fatal septicæmia.

In simple catarrhal empyema of the gall-bladder, organisms are not necessarily present; for instance, in a case in which I recently operated, where a tumour of the gall-bladder had been present for a year, and from which I removed sixteen gall-stones and two ounces of thick muco-pus, Dr. Buchanan and I failed to discover any organisms. In this case the walls of the gall-bladder were not thickened, and the serous coat was free from inflammation. Moreover, there were no adhesions except over the cystic duct, where the largest gall-stone had been impacted. On the other hand, Mr. C. B. Lockwood found streptococci and other organisms (but no amœbæ coli) in an empyema of the gall-bladder.

In acute or phlegmonous cholecystitis the walls of the gall-bladder are swollen and œdematous, and they may be infiltrated with pus. In three out of five of such cases Naunyn found the B. coli communis in the pus. Bonnecken in 1890 demonstrated these organisms in the sac of a strangulated hernia, although there was no perforation. Barbacci has also shown that peritoneal sepsis may occur without perforation of the gut. Though there be no perforation, the spread of infection through the walls of the gall-bladder may occur in these cases, as may virulent peritonitis. Gilbert and Girode found typhoid bacilli in the pus from a case of empyema of the gall-bladder which came on as a *sequence of enteric fever. Gilbert and Dominici also assert that they* produced suppuration in the gall-bladder and liver of rabbits by injecting a culture of typhoid bacilli into the common duct. These biological facts are borne out by the clinical observations of Dr. Murchison and Dr. Hale White, who found evidence of inflammation and ulceration of the biliary passages in well-marked and fatal cases of typhoid fever.

From the foregoing observations it would seem that though the bile-channels and their contents, under ordinary conditions, are free from organisms, their proximity to the intestinal canal, where bacteria abound, renders them liable to invasion; infection does not occur, however, when the organs are healthy, but only under some abnormal condition such as gall-stone obstruction or typhoid ulceration.

Suppurative catarrh of the gall-bladder and bile-ducts.—In the greater number of cases, both of simple empyema of the gall-bladder and of suppurative cholangitis, gall-stones are the primary cause; but hydatid disease and cancer of the ducts may also dispose to suppurative inflammation.

Suppurative catarrh of the bile-tracts must always be a serious affair; though simple catarrhal empyema of the gall-bladder alone, due to obstruction in the cystic duct, is of much less serious import than when it is associated with suppuration of the ducts within the liver.

In catarrhal empyema of the gall-bladder, without invasion of the hepatic ducts, the symptoms will depend on the cause; but, as this is in nearly all cases cholelithiasis, there will be the usual history of gall-stone attacks, followed by a swelling under the liver and by a continued instead of an intermittent pain.

Tenderness is nearly always present in consequence of the local adhesive peritonitis, which is rarely absent.

The tumour, if seen at an early stage, will descend with the liver on respiration, and will be palpable as a rounded swelling. After a time the swelling may become more diffused and general, and the movements during respiration will be less marked, or may cease if the inflammation extend to the abdominal walls. If the suppuration extend beyond the gall-bladder the pus may make its way through the parietes, and an abscess may form either under the ribs or at the umbilicus. For the description of the physical signs see the sections on Tumours of the Gall-bladder (p. 226).

At first the constitutional symptoms may be but slightly marked, and there may be no increase of temperature; though in some cases from the beginning, and in others in the later stages, rigors or chills with fever may point to the formation of pus.

The patient may be driven to bed at an early stage on account of the pain on movement. The loss of appetite and the fever lead to loss of flesh and weight, and yet the case may go on for several weeks, or even months, before relief by operation is sought.

In suppurative cholangitis there is progressive enlargement of the whole liver, which may descend as low as the umbilicus; the swelling *being uniform, smooth and tender on pressure. If the cause be in the* common duct, and the gall-bladder has not previously become contracted, there will be the additional enlargement caused by its distension; but when contraction has taken place, as also when the obstruction is in the hepatic duct, there will be an absence of the signs of empyema of the gall-bladder. Pain may be absent, as in one case, on which I operated, where the disease was dependent on cancer of the common duct; but where it is dependent on gall-stones the pain may be severe and paroxysmal, each attack being accompanied by ague-like seizures and an intensification of the jaundice.

Jaundice is always present, and is both persistent and intense. Continued fever, with occasional rigors and profuse perspiration, is a feature of the disease, and with it rapid loss of flesh and strength.

Pneumonia or pleural empyema not infrequently supervenes. Although the disease often proves fatal, recovery may occur if the cause can be removed at a sufficiently early stage.

In a case of suppurative cholangitis, dependent on cancer of the common bile-duct, which proved fatal in the Leeds Infirmary, the bile-ducts throughout the whole of the liver were found full of pus, the main channels being considerably dilated. If the disease be less acute, the inflammation concentrating itself in some parts of the liver may lead to abscess, which may form a distinct tender swelling and give rise to the usual symptoms and signs of hepatic abscess. For a full account of cholangitis the reader is referred to p. 249.

The treatment of simple empyema of the gall-bladder is almost purely surgical: it consists in evacuating the pus, draining the gall-bladder, and removing the cause if this be possible. If the patient be very ill the operator may have to rest content with cholecystotomy and drainage, leaving the obstruction to be dealt with afterwards. If the case be seen at an early stage, the cause, if removable, should be dealt with at once. The operation yields excellent results, and I can point to a number of patients thus treated who are now quite well. Even in suppurative cholangitis, with distended gall-bladder, cholecystotomy should be performed and free drainage established. Although good results cannot be expected in all cases, an amelioration of the symptoms may be looked for in a fair proportion, and in others complete relief.

If a localised abscess be discovered in the liver it should be opened and drained; and though it is scarcely to be expected that the results of operation can be brilliant in these otherwise almost hopeless cases, yet the chance of permanent benefit is worth snatching at.

Of general means, warm applications to the hepatic region, an initial mercurial purge followed by milder laxatives if required, intestinal anti-

sepsis by bismuth and salol, the relief of pain, if called for, by sedatives, and the treatment of other symptoms as they arise, will afford some amelioration, though the relief will probably be only temporary.

Ulceration, perforation, fistula, and stricture.—These pathological conditions may conveniently be considered together, as they usually, though not constantly, own one origin, namely, gall-stones; moreover, perforation, fistula, and stricture are all accompanied or preceded by ulceration.

Ulceration of the gall-bladder and bile-ducts is found to be present in many though not in all cases where a gall-stone is impacted; and it may help to explain the ague-like attacks which are present in some cases of cholelithiasis and absent from others. Ulceration is generally found also where gall-stones have led to empyema of the gall-bladder or to suppurative cholangitis. The ulcers may be quite superficial, mere abrasions of the epithelial lining, or they may be deeper, extending into or through the other coats. Ulceration is, however, chiefly important from its effects—perforation, fistula, or stricture. Ulceration, or even perforation of the gall-bladder or bile-ducts, may occur independently of gall-stones.

Dr. Hale White (38) described a fatal case of enteric fever in a boy of seventeen, in which there were, besides the usual signs of the fever in the intestine, suppuration and ulceration in the gall-bladder; there was no obstruction to the passage of bile. In some places the walls of the gall-bladder were very thin and almost perforated. Murchison, in his work on the Continued Fevers, says: "The lining membrane of the gall-bladder is very liable to become inflamed in enteric fever without producing very marked symptoms during life"; later, he refers to a case of death from perforating ulcer of the gall-bladder in a youth aged nineteen on the fifteenth day of typhoid fever.

Perforation of the bile passages is not uncommon, but general peritonitis from this cause is rare; as the ulcer advances, extravasation is prevented by adhesive peritonitis.

General suppurative peritonitis from this cause does, however, occasionally occur, leading to a sudden peritoneal catastrophe and, as a rule, to a speedily fatal termination.

In cases of rupture of the gall-bladder from straining, as in cases reported by Dr. Willards (39) and by Mr. Lake (20), there was in all probability some previous disease, such as ulceration, leading to thinning and weakening of the walls of the gall-bladder, and disposing to rupture from slight causes.

Dr. George P. Biggs reports a fatal case of perforating ulcer in a woman who had suffered a month previously from gall-stone colic. The onset was sudden, and was accompanied by cramp-like pains in the upper abdomen, which were rapidly followed by signs of acute general peritonitis. She died on the fourth day of illness. At the autopsy the abdomen was found greatly distended and full of a dark brown, bile-stained fluid having a slightly fæcal odour; the peritoneum was covered with fibrinous exudation. Just inside the orifice of the common bile-duct a large gall-stone was impacted, and at the junction of the gall-bladder and cystic duct a minute oblique perforation was found in the floor of an old ulcer. The cystic, hepatic, and common ducts were all much dilated, the latter admitting a cylinder one centimetre in diameter. The muscular wall of the gall-bladder was hypertrophied, and the mucous membrane thickened from chronic inflammation; near the outlet there was superficial ulceration.

If perforation be recognised and operated on at once, recovery is possible—as in the case of a man aged forty-five, whom I saw with Dr. Braithwaite of Leeds, and who, after symptoms of inflammation in the hepatic region extending over several weeks, suddenly became worse and showed signs of general peritonitis. I opened the abdomen in the right linea-semilunaris and evacuated several pints of bile and pus. The abdomen was washed out, and drainage-tubes were passed, between the liver and diaphragm, into the right kidney pouch and downwards towards the pelvis; the patient recovered and is now in perfect health.

One of the most remarkable cases of perforation of the gall-bladder following typhoid ulceration, successfully treated by abdominal section, is reported by Dr. Monnier Williams and Mr. Marmaduke Sheild (10). The case occurred in a married women, aged thirty-one, who was treated by operation on the fifty-first day of the disease; the gall-bladder was then found to be rigid, thickened, and of a dark plum colour, with a sharply circular sloughy ulcer, the size of a threepenny piece, near its neck; the gall-bladder contained about one and a half ounce of thick offensive pus; the abdomen was washed out, the distended intestines were emptied by puncture, and gauze-packing with drainage was adopted: a complete cure was the result. There seems to be a question whether the case were not one of phlegmonous cholecystitis from the first, but there can be no question as to the brilliant success of the treatment.

In the greater number of cases perforation occurs slowly, as in a case of a feeble, aged woman whom I saw with Dr. Chadwick of Leeds a few days before her death. Jaundice had been present for five years, and at the necropsy a large gall-stone was found lying in a cavity outside of the common duct, but pressing on it. The cavity was shut off from the general peritoneal cavity by adhesion of the neighbouring viscera.

In some cases, as in one reported by Mr. Norton, the primary perforation may lead to the formation of a second cavity bounded by plastic lymph, which in its turn may rupture and lead to fatal peritonitis. The following is a brief account of the post-mortem appearance in the case referred to; the patient was a woman of sixty:—"The body was well nourished, the abdomen was distended, and on opening it much orange-coloured fluid escaped, and general recent adhesive peritonitis was discovered. Just below the liver was a cavity the size of an orange, bounded above by the under surface of the liver, and in front by the thin margin of the liver and the omentum which had been adherent to it. Below, it was separated from the colon by much thickened tissue. On its inner side lay the omentum, and on its outer side, covered by adhesions between the liver and adjacent parts, lay the gall-bladder, which opened into the cavity by an aperture which would admit one or two fingers. The wall of the gall-bladder was much thickened, and several stones half an inch in diameter were found lying in it. *Where the omentum had before been adherent to the anterior* edge of the liver, *forming* the *anterior* wall of the cavity, it had become detached, and thus the bile had escaped into the peritoneum and set up fatal peritonitis. No doubt at one time the gall-bladder, containing gall-stones, had perforated under these surrounding adhesions, and thus the secondary gall-bladder had been formed which in its turn had finally ruptured into the peritoneum. The old gall-bladder was not dilated to any extent."

In several cases I have seen a large gall-stone ulcerate its way quietly, almost without symptoms, into the duodenum or colon, and produce no distress until in the intestinal canal, when all the symptoms of acute intestinal obstruction were produced. Rarely gall-stones have ulcerated their way into the pelvis of the right kidney and set up symptoms of renal stone. Where adhesions form between the gall-bladder and the parietes an abscess may form in the abdominal wall, either over the region of the gall-bladder, at the umbilicus or elsewhere, which, on being opened, discharges pus and gall-stones, and leaves a fistula which, without further treatment, may become permanent, and discharge mucus or muco-pus or bile; sometimes such a fistula may close spontaneously if the obstruction have passed away. Contrary to what one might suppose, fistulas between the bile passages and other hollow viscera in the majority of cases close spontaneously, leaving visceral adhesions: thus the fistulas are but rarely found post-mortem.

A fistula may at times open the way to septic absorption and to death from septic complications. Mucous fistulas are occasionally seen after the operation of cholecystotomy where the obstruction in the cystic duct has not been overcome, or where that duct is the seat of stricture. In one case of this kind with which I am acquainted, the patient has so little inconvenience that she does not think it worth while to undergo any further treatment. In two other cases of mucous fistula dependent on stricture of the cystic duct I removed the gall-bladder, effecting thereby a complete and permanent cure.

Biliary fistula may also continue after cholecystotomy where the common duct is strictured, or where the obstruction is permanent, or has not been removed. In two cases of this kind, dependent on stricture, I connected the gall-bladder to the intestine by means of decalcified bobbins, and then closed the external wound; thus the fistula was cured and the flow of bile restored to the bowel: both patients are now in very good health.

Stricture is probably always the result of ulceration due to gall-stones, and may not manifest itself until the original cause has passed away. If in the cystic duct, it leads to a gradual and almost painless distension of the gall-bladder; if in the hepatic duct, to a gradual increasing jaundice with enlargement of the liver, but without distension of the gall-bladder; if in the common duct, to jaundice, enlargement of the liver and distended gall-bladder; though if the stricture have been caused by gall-stones in the common duct the gall-bladder may be contracted. In one such case (not yet reported), in which I recently operated, the history of gall-stones had extended over a period of eighteen years, and for three years there had been persistent jaundice dependent on stricture of the common bile-duct.

The first and last events are not very uncommon, as will be gathered from the foregoing remarks; but stricture of the hepatic duct is probably very rare, though a fatal case was lately reported.

A form of stricture not commonly described, but which may be found occasionally, is one in the middle of the gall-bladder producing an hour-glass contraction of that ordinarily pear-shaped cavity: in one case I found the upper cavity separated from the lower by a stricture apparently impermeable; both cavities contained gall-stones which were successfully removed.

Needless to say, stricture of the bile passages will scarcely call for diagnosis apart from its cause; though different treatment will be demanded when the disease is recognised at the time of operation.

In stricture of the cystic duct the gall-bladder should be removed, otherwise the symptoms will recur when the wound closes, or there will be a permanent mucous fistula.

As an alternative, the gall-bladder may be "short-circuited" into the intestine, as in the remarkable case reported by Mr. Swain (34). In stricture of the common duct cholecystenterostomy must be performed, not a simple cholecystotomy; otherwise a permanent biliary fistula will certainly be formed.

Acute phlegmonous cholecystitis and Gangrene.—Acute or phlegmonous inflammation of the gall-bladder was described by Courvoisier in 1890 under the name of acute progressive empyema of the gall-bladder; and he stated that it usually leads to a fatal termination in a few days from diffuse peritonitis. Only seven cases are recorded in Courvoisier's voluminous statistics. Potain also says that, besides the ordinary variety of empyema of the gall-bladder, there is an acute empyema of a very grave kind, which is followed by rapid peritonitis and death. In one case, which he describes, death occurred on the second day after the onset of the attack; and although there was no perforation of the walls of the viscus, infection had spread through the coats to the general peritoneal cavity. Osler (28) also refers to it as an extremely rare disease.

A case described by Mr. W. Arbuthnot Lane affords a good example of phlegmonous inflammation which, owing to the secondary peritonitis, simulated acute intestinal obstruction. A man, aged fifty-four years, was suddenly seized with severe abdominal pain immediately after a rather hearty meal. This continued and was accompanied by frequent vomiting: next day the vomiting became less frequent and then ceased; ingestion of food, however, caused much distress and a renewal of the vomiting. The abdomen became much distended, the pain and distension being more marked on the right side. These symptoms increased in severity till the fourth day of illness, when Mr. Lane first saw him. The bowels had not moved since the onset. He was now in a very prostrate condition with a small, rapid pulse and a very distended, painful, and tender abdomen, the hardness and fulness being most distinct about the right hypochondriac region and its vicinity. There was no previous history of gall-bladder trouble nor of intestinal obstruction. From the distended condition of the small intestines and cæcum, and the collapse of the colon on the left side, the case was supposed to be one of obstruction about the hepatic flexure. On opening the peritoneal cavity a very thick layer of firm lymph was found, covering the edge of the liver and extending over the adjacent transverse colon; beyond this part the colon was empty, in marked contrast with the distended condition of the proximal part of the bowel. In immediate relation with the transverse colon and the duodenum, which was also covered with lymph, was found a tightly-distended livid gall-bladder which, though not larger than normal, was evidently very acutely inflamed. The whole of the lymph was carefully removed, and the gall-bladder tapped of its contents, which consisted of a thick muco-pus. The opening was then enlarged, a drainage-tube inserted, and the margins of the wound stitched to the peritoneum. No gall-stone was discovered. The patient made a complete recovery.

The comparative frequency of gangrene in the vermiform appendix might lead one to suppose that gangrenous inflammation of the gall-bladder would not be uncommon; yet it is extremely rare, and so far as I know, the case reported by Dr. L. W. Hotchkiss is the only one recorded. In this case, a boy, aged nineteen, was admitted to the Belle Vue Hospital, New York, with acute peritonitis; it had come on suddenly and was thought to be due to appendicitis, as the pain was most severe over the cæcal region. No previous history of gall-stones was obtainable. Exploration of the abdomen revealed a tumour of purplish hue, very tense and markedly congested; some pus was found on its outer side, and, within it, thin, sticky fluid of a yellowish brown colour, together with a number of gall-stones. The lower end of the gall-bladder was almost black; its walls were extremely thin and apparently gangrenous. Death occurred seven hours after the operation—thirty-four hours after the onset of the attack; the vomiting, rapid pulse, and high temperature continuing to the end.

In order to explain the occurrence of gangrene three factors have to be borne in mind: (*a*) thrombosis of the nutrient vessels; (*b*) bacterial infection; (*c*) absence of drainage and consequent tension. The two latter are present in both gall-bladder and appendix inflammation; but the first factor is more frequent in the vermiform appendix, which is supplied by one nutrient artery only; whereas the gall-bladder has a very free blood-supply, not only through the branches of the cystic artery, but also through their anastomoses with the hepatic, where the organ is fixed to the liver.

In Dr. Hotchkiss' case there was an abnormal circular constriction of the gall-bladder with lymph infiltration, which was apparently sufficient to cut off the blood-supply from the extremity of the part.

Although the disease is usually associated with gall-stones, Mr. Lane's case would seem to prove that acute cholecystitis may arise independently of them; in this it resembles appendicitis, which may occur without the presence of foreign bodies.

Typhoid fever may give rise to it, as in the case recorded by Dr. Monnier Williams and Mr. Marmaduke Sheild, which is referred to in the section on Ulceration.

Whatever be the cause, the disease usually manifests itself somewhat suddenly with pain on the right side of the abdomen, which rapidly becomes general. A rapid and feeble pulse, quick thoracic breathing, fever, intense general depression, marked tenderness, especially over the right side of the abdomen, rapidly increasing tympanites, persistent vomiting, and an extremely anxious expression of countenance, are its chief symptoms. The acute peritonitis, significant of the disease, may be localised at first; but later it becomes general. Jaundice may or may not be present; and although an elevation of temperature is usual, it is by no means constant, and affords but slight assistance in diagnosis or prognosis. If the disease be of the very acute or gangrenous variety, death speedily occurs; but if of the subacute form, an abscess may form round the gall-bladder, and the peritonitis may become localised; the disease then resembles a perityphlitic abscess in its course.

The diagnosis of phlegmonous cholecystitis practically resolves itself into a diagnosis of the cause of an acute peritonitis starting on the right side of the abdomen. Although this may be due to perforation of the stomach at or near the pylorus, to perforation of the duodenum or ascending colon, to perforation of the gall-bladder or bile-ducts, or to some other such peritoneal catastrophe, the chief affection with which it is likely to be confounded is acute appendicitis.

In appendicitis the pain begins at a lower point in the abdomen and passes towards the umbilicus, whereas in gall-bladder mischief it begins below the right costal margins, and passes towards the epigastrium and back to the right scapular region. In the one case the most acutely tender spot will probably be over the cæcum; in the other it is over the region of the gall-bladder. The symptoms of acute peritonitis and paralytic obstruction of the bowels are common to both. The appendix may be abnormally situated under the right costal arch. Fortunately, the treatment by exploratory incision is that appropriate to any one of the various conditions mentioned.

Relief of pain by subcutaneous injections of morphine will probably always be demanded as a primary measure; and as it is clearly impossible to make a diagnosis of this serious malady within the first few hours, warm applications, absolute rest, the stoppage of feeding by the mouth (unless it be in very small quantities), and the relief of symptoms as they arise, must be our temporary measures; but as soon as the diagnosis of phlegmonous cholecystitis can be established, and it is found that the patient is getting worse rather than better, an exploratory incision should be made, and the gall-bladder incised and drained, the cause, if any obvious cause be found, being then removed. If, however, gangrene be discovered, the gall-bladder should be removed, the indications for that measure being as distinct as in the case of a gangrenous vermiform appendix. If, in subacute cases, the inflammation becomes localised, and a swelling with tenderness be found beneath the right costal margin, incision and drainage is called for; at the same time cholecystotomy may be performed, and if gall-stones be present in the gall-bladder or ducts they may be removed. If the patient be too ill to bear a prolonged operation the latter procedure may be left to a subsequent occasion.

TUMOURS OF THE GALL-BLADDER AND BILE-DUCTS.—If by tumour be understood new growth, then tumours of the gall-bladder and bile-ducts are not common; but if we accept the usual interpretation of the word, and call all enlargements tumours, we shall find them by no means rare; the greater number depend directly or indirectly on gall-stones.

The following classification includes the chief tumours of the gall-bladder and bile-ducts:—

I. Tumours of the Gall-bladder.
  A. Distension: (*a*) with bile; (*b*) with gall-stones; (*c*) with mucus, "hydrops"; (*d*) with pus, "empyema."
  B. New growths. (*a*) Malignant; (*b*) Simple.
II. Tumours of the Bile-ducts.
  A. Distension.
  B. New growths. (*a*) Malignant; (*b*) Simple.

I. Tumours of the gall-bladder.—*Etiology.*—The gall-bladder may become hard and almost calcified by the deposit of lime salts in its walls in consequence of disease of its mucous membrane. Usually it can then be felt under the liver margin as a hard nodule, though it seldom forms a tumour of any size. Though a considerable collection of gall-stones, or one large concretion contained in the gall-bladder, may cause a palpable tumour, this is rare; the swelling, as a rule, is due to distension of the gall-bladder in consequence of an obstruction of the lumen of the ducts by gall-stones, so that the escape of the secretions is prevented. If a gall-stone, in passing down the cystic duct, become impacted, so as to block the passage, the gall-bladder gradually becomes distended with mucus, and a tumour is formed. If a concretion be impacted in the common duct the gall-bladder may be distended with bile for a short time, though if the obstruction continue mucus will replace the bile.

Stricture or tumour of the cystic or of the common duct may produce distension of the gall-bladder; so also may hydatid disease, movable kidney and malignant growth lying outside the bile-ducts but pressing on them.

If the symptoms be acute and associated with inflammation, the contents of the gall-bladder may become purulent and a so-called empyema be formed. In certain cases of empyema the size of the tumour may be increased by the formation of pus outside the gall-bladder. The pus may then lie in an irregular cavity either in the liver or below it, but shut out by adhesions from the general peritoneal cavity.

Of the tumours dependent on new growth, so-called, "cancer of the gall-bladder" is the most important; innocent growths, except of inflammatory origin, are excessively rare.

Cancer of the head of the pancreas is usually associated with a perceptible tumour of the gall-bladder, as the new growth embraces and obstructs the termination of the common duct and thus causes retention of secretions.

Signs.—Enlargements of the gall-bladder may vary from a tumour just perceptible to the touch to one of such a size that it may resemble an ovarian cyst, as in cases reported by Kocher and Lawson Tait; though an enlargement of greater size than a large pear is exceptional. The same tumour may also vary in size at different times—a variation frequently found in gall-stone obstructions. The symptoms of tumour of the gall-bladder depend for the most part on the cause, and consequently vary considerably—being at times slight and unimportant, at times both urgent and serious.

The gall-bladder, as a rule, enlarges downward and forward in a line which, drawn from the ninth or tenth costal cartilage, crosses the linea alba a little below the umbilicus; but the position of the tumour varies with the size of the liver. When this organ is of normal size the neck of the gall-bladder is opposite the ninth costal cartilage: whereas when the liver is enlarged the gall-bladder will be pushed down so that the neck of the tumour may be opposite to the umbilicus, or even below it. If uncomplicated it will have a smooth, rounded and pear-shaped outline, the larger end below being quite free and movable from side to side, the upper end being fixed and passing under the lower margin of the liver at the fissure of the gall-bladder.

A distinct sulcus between the liver and gall-bladder is nearly always perceptible to the touch: if the warm, flat hand be laid over the right side of the abdomen, and the patient be told to take a deep breath, the tumour and the liver will descend together and pass under the fingers.

Bimanual palpation will frequently throw additional light on the case; the right hand is to be placed in front of the abdomen, and the left over the right loin, and gentle pressure made forwards. In other cases additional information may be obtained by placing the patient in the genu-pectoral position, and passing the flat hands round the abdomen from behind, when a tumour of the gall-bladder will rest directly on the hands;

on deep inspiration it will be felt to move just beneath the abdominal walls: the upper surface of the liver is also capable of palpation in this way. The sac, as a rule, is far too tense for fluctuation to be felt, though at times, when it is less tense, this sign may be obtained. In some of the larger swellings a thrill, almost like the hydatid fremitus, may be felt on gently flicking the tumour with the finger-nail. Percussion by no means always discovers dulness coextensive with the tumour, and is especially deceptive if the surrounding intestines be distended: dulness on percussion is therefore a very variable sign; palpation will be found more trustworthy. Inspection of the abdomen, with the patient recumbent, will at times show the tumour descending on respiration; but this sign is usually to be observed only in thin patients and in cases uncomplicated with inflammation. When there is inflammation and matting of the adjoining viscera, a fixed swelling, dull on percussion, and decidedly tender, may be seen over the right hypochondrium. Tenderness on palpation is a variable symptom, depending on the presence or absence of local peritonitis; as a rule it is absent in uncomplicated enlargements of the gall-bladder.

Jaundice may accompany tumours of the gall-bladder, both being dependent on the same cause—the blocking of the common bile-duct. Although not absolutely pathognomonic of malignant disease, the combination should always raise a suspicion of cancer of the head of the pancreas, or of the liver or bile-ducts, especially if it be associated with great loss of flesh and strength, and with absence of characteristic gall-stone pain.

In a considerable number of cases I have observed distension of the gall-bladder with jaundice to be associated with malignant disease; but much less often the combination of tumour, jaundice, and gall-stones. The explanation of this apparent anomaly is that the gall-bladder frequently becomes diminished in size as the result of gall-stone irritation, so that when the common duct becomes blocked by a stone jaundice occurs, but the previously shrunken gall-bladder is unable to expand. If, however, the common duct become blocked by gall-stones before the gall-bladder has contracted and formed adhesions, the combination of jaundice and tumour may occur. If, when the common duct is blocked by a new growth, the gall-bladder has not been subjected to previous irritation, and has not therefore become contracted, it will distend at once. Thus, in malignant disease of the head of the pancreas we usually find the combination of jaundice with tumour of the gall-bladder.

Gall-bladder tumours usually contain mucus, occasionally pus, rarely bile. In all cases where the cystic duct is obstructed and inflammation has not followed, mucus alone is present; though, when inflammation coexists, pus or muco-pus may be found. In obstruction of the common duct by gall-stones, the gall-bladder, though usually contracted, may be found distended by bile at first and by mucus later. As a rule, however, the swelling subsides more or less rapidly, the gall-bladder shrinks, and no tumour persists. Where the obstruction becomes absolute, as in malignant disease of the head of the pancreas, the tumour formed is persistent; and although the block is in the common duct, bile soon ceases to reach the gall-bladder, and the tumour is always found to contain mucus only.

Diagnosis.—Tumours of the gall-bladder may have to be distinguished from—(*a*) movable right kidney, (*b*) tumour of the right kidney or of the suprarenal capsule, (*c*) tumour of intestine or fæcal impaction, (*d*) tumour of liver, (*e*) pyloric tumour, (*f*) abnormal projection of liver. The diagnosis of enlargement of the gall-bladder from movable right kidney in thin persons is as a rule easy, but in those who are stout, or have tense or strong muscular abdominal walls, difficulties may and do arise which, however, can usually be overcome by examination under an anæsthetic (*vide* art. "Nephroptosis," p. 338).

These enlargements resemble one another in that they form moderate-sized, distinctly-defined, smooth, rounded, and movable tumours on the right side of the abdomen, which descend on inspiration. The previous history may throw light on the individual case, especially if there have been definite cholelithic attacks or jaundice. By inspection of the abdomen a gall-bladder tumour is often apparent, moving rhythmically with the respiratory movements when the patient is recumbent; a floating kidney can rarely be so detected.

The general outline of the tumour, as detected by palpation, may afford valuable assistance, thus, in distension of the gall-bladder, the tumour formed is pear-shaped, with the apex towards the fissure of the gall-bladder, and its long axis in a line from about the tip of the ninth costal cartilage downwards, forwards, and inwards towards a point a little below the umbilicus. In floating kidney, especially in patients with lax abdominal walls, the tumour may be grasped and its characteristic shape made evident. Should adhesive peritonitis accompany the gall-bladder condition there will be tenderness and pain on pressure over the tumour, especially near its apex. These signs are rarely if ever present in floating kidney.

The gall-bladder tumour on manipulation can usually be moved to a limited extent inwards and outwards; but under no circumstances can it be depressed into the pelvis. On relieving the pressure it tends to resume its old position under the liver. Floating kidney generally has a wider movement; it can be depressed into the pelvis, and, when relieved of pressure, it tends to pass towards the right loin, especially when the patient is recumbent.

A valuable diagnostic sign is the sulcus often felt between the lower margin of the liver and the gall-bladder tumour. This can usually be felt when the warm flat hand is placed over the upper part of the swelling, and the patient breathes deeply.

In the case of renal tumour, as well as in movable kidney, by distending the intestine with gas the kidney will be pressed back into the loin; but the gall-bladder will be pushed up towards the liver and made more prominent. The last test is usually also sufficient to enable a diagnosis to be made between a distended gall-bladder and a tumour of the right suprarenal body; but this point is not always to be relied upon. In a case I saw with Dr. Kebbell of Flaxton, Ziemssen's test pushed the swelling upwards; and on performing abdominal section, a sarcoma of the suprarenal capsule was found and removed. The explanation was that the colon was fixed below the growth and pushed it up when the bowel was distended.

In tumour of the intestine or of the pylorus the associated symptoms are usually sufficient to enable us to make a diagnosis; but, when in doubt, distension of the stomach or bowel with gas, or examination under an anæsthetic, will help to clear it up. Tumour of the liver itself—whether cancer or hydatid disease—may be almost indistinguishable from one of the gall-bladder; though the presence of nodules in the liver, with the history and other symptoms of malignant disease, will usually be sufficiently distinctive in cancer, while the less localised and more generally fluctuating swelling, together with the longer history and absence of pain, will distinguish hydatid tumour. It should not be forgotten that the right lobe of the liver may have an abnormal projection either in the site of the gall-bladder or to the right of that position, and may thus at first be mistaken for an enlarged gall-bladder; but the absence of symptoms, together with careful bimanual palpation, will usually enable a correct diagnosis to be made, and, as Professor Riedel has pointed out, the gall-bladder may frequently be felt apart from the swelling. Puncture with an exploring syringe would, of course, give valuable information; but, as this measure is not devoid of risk, it should not be lightly undertaken; death has occurred on more than one occasion as a direct result of this apparently slight operative procedure. If it be decided to employ an exploring needle, the aspirator should always be used in order that the tense cyst may be emptied; otherwise leakage from the puncture is almost certain to occur.

In cases of doubt, especially where the symptoms demand interference, exploration of the tumour through a small abdominal incision can be undertaken with very little risk; and further treatment, if called for, can be readily carried out at the same time.

Cancer of the gall-bladder is by no means frequent, and as a primary affection is somewhat rare. Musser has collected the chief cases. It is usually secondary to gall-stones or to cancer of adjoining organs, and in the latter case it is hardly amenable to surgical treatment. It is an unfortunate circumstance that very few of the specimens of so-called cancer of the gall-bladder have been submitted to careful microscopic examination; but of those that have been so examined, the growth has been found in the form of cylindrical epithelioma. The disease occurs as a uniform thickening of the walls of the gall-bladder, and in the centre of the mass a cavity containing gall-stones is often found. It may attain the size of a large pear.

Symptoms and Signs.—If the growth be primary, there will be the history of a more or less rapidly-growing tumour developing under the right costal margin; it is accompanied by a sense of discomfort shortly changing to pain which is often worse at night, and which, though at first localised to the right hypochondrium and epigastrium, usually extends round the side to the right infrascapular region. When the enlargement is first noticed, it is felt as an egg-shaped swelling beneath the liver, descending with that viscus on inspiration. The tumour is hard to the touch, and very slightly or not at all tender to pressure. At a later stage it becomes more fixed and more diffused, and nodules may form and be felt on its surface. As the growth extends, it invades the liver and sometimes the duodenum and stomach.

Dissemination is rare. When it occurs, nodules may be found in the liver, and generally over the peritoneum; in such cases ascites appears. The lymph-glands in the hilum of the liver usually become affected. As the hepatic or the common bile-ducts are or are not invaded, so will be the presence or absence of jaundice, but in nearly half of the cases some degree of icterus will be found as the disease advances. Interference with the action of the bowels, even to partial or complete obstruction, occurs at times. General failure of health, continued wasting with loss of strength, ascites, and marked cachexia characterise the later stages. If gall-stones be present there will be the usual antecedent history of cholelithiasis. I have known the combination of gall-stones and cancer of the gall-bladder to be unaccompanied by jaundice. Where gall-stones with jaundice complicate cancer of the gall-bladder, exacerbations of pain will usually be accompanied by rigors and fever ("ague-like attacks"), with an intensification of the icterus; moreover, in such cases petechiæ in the skin and hæmorrhage from the nose and rectum usually appear.

Diagnosis.—Cancer of the gall-bladder may usually be diagnosed by the progressive character of the disease, and by the presence of the characteristic hard tumour; but it is by no means always easy to diagnose cancer from a tumour formed by matted intestines, due to local peritonitis in the neighbourhood of the gall-bladder.

In a doubtful case of this kind, in a woman of fifty, I opened the abdomen, and found what appeared to be a malignant tumour of the gall-bladder, which was punctured in several spots with an exploring syringe. Finding it firm and hard I concluded it was malignant, and as it was too extensive for removal I closed the abdomen, thinking nothing more could be done. The patient, however, recovered forthwith, is now well, and has no remnant of her tumour. In all probability it was an inflammatory swelling associated with gall-stones. In another case of tumour where there was a suspicion of malignancy, an abscess of the liver, containing thirty gall-stones, was opened, with marked relief, though only for a time; death supervened four months later, when cancer was found. When in doubt exploration is advisable, as treatment may be carried out at the same time.

That cancer of the right suprarenal body may afford a difficulty in diagnosis is shown by the case referred to in the chapter on tumours of the gall-bladder. The same difficulty applies to cancer of the pylorus, which, however, is accompanied for the most part by characteristic stomach symptoms.

Treatment. — The alleviation of symptoms, especially of pain by sedatives, is practically all that can be done, except in those rare cases where the disease is limited to the gall-bladder, when cholecystectomy may be performed. That cholecystectomy is occasionally practicable in cancer of the gall-bladder, is proved by a case I reported at the June 1896 meeting of the Royal Medical and Chirurgical Society, in which I had removed from a middle-aged woman not only the whole of the gall-bladder but a considerable portion of the adjoining right lobe of the liver also; the patient made a good recovery. The disease had started at the neck of the gall-bladder behind an impacted gall-stone. Microscopic examination showed the growth to be epithelioma.

II. Tumours of the bile-ducts rarely form projections so large as to be distinguished through the abdominal walls. Tumour, however, in such cases, as a rule, is present sooner or later on account of the obstruction in the ducts and secondary distension of the gall-bladder; or if the gall-bladder be contracted, the common duct may be dilated to such a size as to form a cystic tumour presenting all the characteristics of a distended gall-bladder

Terrier describes four cases in which an external fistulous opening was established from the common bile-duct. In three of these the duct was much distended, and formed a distinct abdominal tumour. The first case was one in which median laparotomy was performed for the removal of a swelling regarded as a cyst of the pancreas. The nature of this swelling having been revealed by the discharge of bile after puncture, a small portion of the wall of the cyst was excised, and the edges of this opening were attached to the external wound. The biliary fistula thus formed bled freely for some days after the operation, and afterwards suppurated. The patient died on the twenty-ninth day from anæmia and exhaustion. In the second case the much-distended duct, which had been regarded as a hydatid cyst of the liver, was exposed by laparotomy, incised, and attached to the wound in the abdominal wall. The patient died on the eighth day from collapse. In the third case the dilated duct was opened and stitched to the external wound under the supposition that the tumour was a distended gall-bladder. In the original report of the fourth case it is not clearly stated whether the duct was distended or not. In this instance the hepatic portion of the divided duct was fixed to the surface of the abdominal wall, after removal of the gall-bladder, the cystic duct, and a small portion of the liver for cancer. The patient did well for some time after the operation, but died six weeks later from cachexia. In his comments on these records, Terrier points out that in two of the cases the distension of the bile-duct, though clearly due to obstruction, was not associated with lithiasis. In the third case the duct was found completely obstructed at its intestinal orifice by a small calculus. In each instance of distended bile-duct the gall-bladder was much shrunken, and its walls were sclerosed and surrounded by cicatricial tissue. Although hitherto the results of choledochostomy have always been fatal, probably in consequence of the fact that extreme distension of the bile-duct is often accompanied by infection of the biliary passages, it would be well, Terrier thinks, to reserve our opinion on the prospects of the operation. As yet very little information can be obtained on this subject; cases of distension of the common bile-duct are very rare, and those in which surgery has intervened are still rarer. An extremely interesting case is reported by Mr. W. P. Swain (34), in which he connected a dilated bile-duct to the jejunum by one of Murphy's buttons. The size of the tumour, which occurred in a girl of seventeen and was associated with gall-stones, may be gathered from the fact that over seven pints of fluid were withdrawn from it at the time of operation. Three months later the patient was progressing satisfactorily, save that the temperature rose occasionally, and that the button had not been passed.

Two forms of new growth have been found primarily in the bile-ducts: (*a*) Cylindrical epithelioma, (*b*) Papilloma. The latter is probably an earlier stage of the former, and is rare.

Mr. Bennett removed one from the common duct of a woman aged fifty-eight, in St. George's Hospital; the specimen was shown at the Pathological Society of London in May 1894. The growth was white and somewhat granular to the naked eye, and it was in immediate relation with an impacted gall-stone. Microscopically it resembled a glandular polypus of the intestine. The papilloma was apparently due to the irritation of the stone, which from the history appeared to have been impacted for two months.

Cancer, in most if not in all cases, is secondary to gall-stones; though, as in a case on which I operated and which I reported at the Clinical Society in October 1889, they may not always be found, as the stones may have passed into the bowel before the operation

Although these tumours are usually seen in the common duct, they may occur in the cystic or in the hepatic duct. If forming in the cystic duct, jaundice will be absent at first, coming on later when the growth advances so far as to press on the common duct and obstruct the passage of the bile. The gall-bladder enlarges at an early stage, and this will probably be the earliest sign; pain may be absent unless gall-stones exist, when the usual spasmodic pain will occur so long as the muscular coat of the gall-bladder retains its contractile power.

When the growth is in the common duct jaundice comes on at an early stage, and persists throughout, the liver gradually increasing in size, and the gall-bladder also enlarging ultimately.

Suppurative cholangitis is apt to supervene, in which case the course is more acute, and is accompanied by fever, ague-like attacks, and rapid loss of flesh and strength.

If the tumour form in the hepatic duct, jaundice will be the earliest symptom, and the case will resemble one of obstruction in the common duct, except in the absence of enlargement of the gall-bladder. Needless to say, the disease is uniformly fatal though operation may delay the final catastrophe. The growth is usually a cylindrical epithelioma.

Besides primary carcinoma of the bile-ducts, malignant disease may invade them, by direct continuity, from the gall-bladder, from the pancreas, or from the liver; when the symptoms are those of growth of the bile-ducts engrafted on the original disease.

The diagnosis of new growth from gall-stones in the bile-ducts is practically impossible; the symptoms are the same, and in fact the two frequently coexist. *The absence of pain and the rapid deterioration of health may afford a little help, but in some cases the pain is as* acute as in cholelithiasis.

Cystic dilatations of the bile-ducts are indistinguishable from enlargements of the gall-bladder, for which indeed they are usually mistaken until the abdomen is opened.

The operative treatment of these tumours is in its infancy, and thus far has not proved very satisfactory. Any growth should be removed if possible; but, where this is impracticable, the dilated gall-bladder may be opened, stitched to the surface, and drained; or better still, it may be drained into the duodenum or jejunum by making an anastomosis by means of a Murphy's button. Choledochostomy in cystic dilatation of the bile-ducts has not yielded good results; whereas the establishment of an anastomosis between the cyst and the intestine, so far as our experience has gone, has been so satisfactory as to establish some claims to our attention as the best method of treatment.

In operating, it is important to bear in mind that the cause of dilatation of the ducts may be a removable one, such as gall-stones; and if so, and if removal be practicable, that should be done.

GALL-STONES.—The importance of this subject may be gathered from the fact that post-mortem records on Europeans of all ages and of both sexes prove that gall-stones are present in from 5 to 10 per cent. In Strasburg the record is 12 per cent (Schroeder), in Kiel 5 per cent, and in Manchester 4·4 per cent (Brockbank); but as these statistics are taken from hospital patients representing the working classes, who are the least subject to gall-stones, the estimate is probably below the mark. On the other hand, in India, and in the East generally, gall-stones are said to be extremely rare; one or two cases only have been recorded.

Pathology and Etiology.—Gall-stones, which, when small, are often spoken of as biliary sand, may vary from a concretion just perceptible to the naked eye up to a mass the size of a tennis ball, or even larger. They may be round, egg-shaped, barrel-shaped, elongated with pointed ends, or angular; the surface being smooth, mammillated, or irregularly faceted. Gall-stones, when large, are usually single, but when small or moderate in size, several hundreds may be present; for instance, in March 1895 I successfully removed by cholecystotomy no less than 720 stones from the gall-bladder and dilated cystic duct of a woman aged fifty-six.

Their colour is variable; in some cases it is white or gray, in others very dark, or even quite black; the usual colour is a dark yellow or brown. In consistency they are ordinarily firm, but may without much difficulty be fractured by pressure between the thumb and forefinger, the fracture being crystalline; but they may be as hard as a lithic acid calculus, or as soft as half-set putty. The chief constituent of gall-stones is cholesterin, which always occurs in the crystalline form; but bile pigments, bile salts, lime, mucus, degenerated epithelium, and, rarely, foreign bodies may enter into their composition.

Margarate, stearate, and palmitate of lime, combined with mucus, usually form the cement which binds the cholesterin crystals together to form a concretion.

Gall-stones formed almost entirely of bile pigment may be seen; and on two occasions I have found soft concretions of this nature in large numbers in the hepatic ducts within the liver. Since cholesterin is the chief constituent of gall-stones, our attention in considering their formation must be directed chiefly to the physiology of this monatomic alcohol, which occurs, normally, not only in the blood, but also in the various organs of the body.

Although cholesterin is always present in the bile in a proportion, according to different authors, varying from ·045 to 1·18 per cent, very little is known of the processes which determine its existence. As there is no proof that the liver excretes cholesterin from the blood, or that it is a result of hepatic metabolism, we are driven to the conclusion that it is formed in the bile-ducts or gall-bladder; and, as it is found in other passages lined by mucous membrane where there is no bile near, there is no reason to believe that it is formed from any constituent of the bile, but rather that it is a product of the epithelium of the bile passages—that, in fact, it is a secretion of mucous membranes generally [*vide* p. 34].

Why, when ordinarily present in all persons, cholesterin should form concretions in some and not in others, may be dependent on several causes; possibly in some cases cholesterin occurs in positive excess, while in others there may be a diminution of the bile salts which should hold the cholesterin in solution, or it may even be precipitated from solution.

There is no doubt that catarrh of the mucous membrane of the bile passages increases the amount of cholesterin present, and that the longer bile remains in the gall-bladder the more cholesterin it will contain. Anything, therefore, which causes stagnation of bile may dispose to gall-stones; on the other hand, whatever leads to a regular emptying of the bile passages will tend to clear out such detritus as cast-off cells and incipient collections of cholesterin crystals and mucus, and thus to prevent the formation of gall-stones. Among the remoter causes we must consider age, sex, habits, dress, diet, diathetic conditions and disease.

Age.—Although gall-stones may occur at any age, and even in the newly-born (Portal and Lieutaud), they are rarely found under the ages of 25 or 30; Schroeder says that under the age of 20 the percentage is

2·4; from 20 to 30, 3·2; from 30 to 40, 11·5; from 40 to 50, 11·1, from 50 to 60, 9·9; and over 60, 25·2 per cent.

Sex.—Gall-stones occur more frequently in women than in men. Schroeder finds that in Germany they are found in 20 per cent of female, and in 4·4 per cent of male necropsies. Out of 228 autopsies on women in the Manchester Royal Infirmary, Dr. Brockbank found 18, and out of 542 post-mortem examinations in men, 16 cases of gall-stones, which gives 7·9 per cent in female, and 2·9 per cent in male subjects.

Pregnancy would seem to be a factor in the causation of gall-stones, as, in a large series of cases, 90 per cent of women affected had been pregnant. The wearing of corsets, which tend to force down the front of the liver, and to depress the fundus of the gall-bladder, is probably a distinct etiological factor, especially when combined with want of exercise.

Habits.—Want of exercise, whether from lethargy or from necessity, as in some forms of chronic heart disease, leads to stagnation of bile in the gall-bladder, and to the deposition of cholesterin; since the gall-bladder is unaided in its expulsive efforts by the abdominal muscles.

Catarrh of the gall-bladder and bile-ducts probably acts as a cause in two ways; in the first place, it leads to stagnation of bile by paresis of the muscular coats of the passages, and in the second place by increasing the amount of cholesterin present.

Diet.—The following facts go far to prove that diet exercises a strong influence in the formation of gall-stones. It seems probable that free cholesterin in the bile passages is due, in many cases, to the deficiency of the solvents of it in the bile, these solvents being the glycocholate and taurocholate of soda which arise from the metabolism of nitrogenous foods. If the supply of nitrogen in the food be limited, the bile salts will be diminished and cholesterin may be precipitated. This may serve to explain the presence of gall-stones in gouty persons who on account of the lithic diathesis limit their intake of nitrogen. The larger consumption of farinaceous food in Germany may also serve to explain the greater prevalence of gall-stones there than in England, where meat enters more extensively into the dietary. In diabetes, when nitrogenous food is prescribed, gall-stones are rarely found.

Thudichum in his work on gall-stones states that he cannot find any recorded instance of the discovery of gall-stones in the wild carnivora; though on two occasions they have been found in the gall-bladders of domesticated carnivora. On the other hand, Brockbank could find no evidence of their occurrence in wild herbivora, though at times they are found in domesticated horses, cattle and sheep, as well as in pigs. Moreover, in pampered dogs fed on farinaceous foods they are found occasionally. In man who is omnivorous they occur in from 5 to 12 per cent.

It will thus be seen that in those who take an abundance of albuminous materials in their food, and where, therefore, the bile salts are in sufficient quantity, there is little tendency to the deposition of cholesterin; whereas when little albuminous food is taken, and the bile salts are presumably insufficient to hold the cholesterin in suspension, gall-stones form, this tendency is aided by insufficient exercise, as in stall-fed cattle, pampered dogs, and indolent men. The formation of some gall-stones containing lime may possibly be caused by drinking hard water, but this is by no means proved. An insufficiency of diluent drinks may possibly act as a cause, and I think I have found this to be a factor in some cases.

Symptoms.—In discussing the symptoms of cholelithiasis we must note, in the first place, that gall-stones may be found after death without having produced any symptoms during life. In such cases they are as a rule in the gall-bladder, and not in the ducts; and there are no signs of irritation in the shape of adhesions. But more than this, there can be no doubt that even a large gall-stone may ulcerate its way into the bowel, and produce symptoms of intestinal obstruction, with few or no signs to indicate that such serious organic mischief has been going on. It follows, therefore, that in considering cases of intestinal obstruction, gall-stones cannot be excluded, though there has been no symptom of cholelithiasis. It is just possible that as some persons may pass urinary stones with few or no symptoms, so others may pass small biliary stones; this, however, has yet to be proved, and in the meantime it is difficult to explain why in some persons gall-stones should produce such serious trouble and in others none at all.

In certain cases there may be a history of dyspepsia, with depression of spirits and a feeling of discomfort or weight, or even ill-defined pains over the right side of the abdomen; but an entire absence of those characteristic symptoms which give definiteness to diagnosis.

The ordinary symptoms of cholelithiasis are paroxysmal attacks of pain which, occurring at irregular intervals, often without apparent cause, start in the right hypochondrium or in the epigastrium, and radiate thence over the abdomen and through to the right scapula. The attacks are often accompanied by sickness or vomiting and, if severe, by collapse They may be followed by jaundice with its well-known symptoms, but this is frequently absent. At times a feeling of fulness in the right hypochondrium accompanies the attack; but the formation of a tumour does not occur as a rule unless the ducts are blocked. Accompanying these special symptoms will usually be found much depression of spirits, want of appetite, dyspepsia, and loss of weight.

According to Naunyn, there is a regular and an irregular form of the disease. The former occurs where the calculi are simply lodged in the gall-bladder, or the stones pass along the ducts; the latter is seen when there is infectious angiocholitis, with abscess in the liver, fistula, and other complications (see sections on Inflammatory Affections of the Gall-bladder and Bile-ducts).

The following symptoms will be considered in detail:—

(*a*) *Paroxysmal pain.*—For the most part the patient complains of pain under the right costal margin or in the epigastrium, whence the pain radiates over the abdomen and to the right scapula; but in some cases the pain radiates to the left shoulder. These attacks come on suddenly, when the patient is apparently quite well; and usually end by causing nausea or an attack of vomiting. The vomiting leads to relaxation of the duct, and if the gall-stone be small it may pass on and thus end the attack. The seizures come on without apparent cause, although at times they may appear to be caused by exertion or by taking food. Not infrequently, after an attack has passed off, a dull aching is felt for some time, perhaps until another seizure.

(b) *Vomiting.—Though as a rule the vomiting is paroxysmal, it may be almost continuous, and so of itself* prove dangerous. In one case of this kind, on which I operated at Sunderland, the patient was so weak from persistent vomiting that I feared she could scarcely bear the operation I had gone to perform; and even after the cause of irritation had been removed, the vomiting persisted for days: ultimately, however, she made a satisfactory recovery. In another case which I saw in the south of Ireland the vomiting had been so incessant that the patient had been fed almost solely by nutrient enemas for six weeks before I operated; and even afterwards, though the operation was satisfactory and the after-progress all that could be desired in other respects, the emesis persisted for a fortnight, and ultimately proved fatal from sheer exhaustion. The vomiting as a rule occurs towards the end of a seizure, and in fact frequently determines its cessation. In such cases the stomach contents are first rejected, after which, if the common duct be free, bile is vomited; at times I have even seen the severe vomiting become stercoraceous.

(c) *Collapse.*—On several occasions I have seen patients so profoundly collapsed by attacks of cholelithiasis as to lead to a difficulty in diagnosis; the case being more like one of perforation of some abdominal viscus or some intra-abdominal hæmorrhage: but the history of previous seizures, and of the onset of the present attack, will usually help us to arrive at a correct diagnosis. The acute agonising pain may of itself cause death, as in the case of a lady whom I saw in consultation, when gall-stones were diagnosed. The next attack of pain unfortunately proved fatal, and at the autopsy a gall-stone was found half extruded into the duodenum.[1]

Not only may the agonising pain of a single attack prove fatal, but repeated attacks of pain occurring one after the other, without sufficient interval for recovery, may produce very serious illness, or even death by exhaustion.

(d) *The formation of a tumour* in the region of the gall-bladder is seldom seen in acute cases; yet it may be noticed with each attack, and it is then due to the violent contraction of the muscular walls of the gall-bladder on its contents. It is, however, a frequent sign in the more chronic cases, as is fully discussed in the section on Tumours of the Gall-bladder.

(e) The presence of *gall-stones in the motions* after an attack is valuable evidence, but their absence does not negative cholelithiasis. I have operated on many cases and found gall-stones where none had at any time been detected in the motions, although diligently sought for.

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[1] Such a case, in a young and healthy married woman, occurred some years ago in my own practice: the stone had passed about four-fifths of the way down the common duct. There was no other morbid condition.—ED.

The way to search for gall-stones is to let the patient pass the motion into a solution of carbolic acid, to have it well stirred, and then to pass it through a fine sieve with about $\frac{1}{16}$ inch mesh.

(*f*) *Jaundice.*—So long as the gall-stones are in the gall-bladder or cystic duct there is nothing to prevent the bile from passing down the common duct into the intestine; but should the gall-stones be impacted in the common duct, the passage of the bile is obstructed, and jaundice ensues. Intermittent jaundice may also occur if a small gall-stone in the common duct act as a ball-valve (Fenger).

In these cases a decision concerning operation is difficult; chronic jaundice too often indicates malignant disease, and not only do patients with cancer bear operations badly, but when jaundice is associated with it there is the same tendency to persistent oozing of blood from the wound after operation as there is to spontaneous hæmorrhage where no operative measures have been undertaken.

(*g*) *Ague-like attacks.*—Dr. Ord drew attention to the production of intermittent pyrexia by gall-stones, and stated that his attention had been first called to this symptom by some remarks of the late Dr. Murchison on a case of a distinguished medical officer who, after his return to England, was attacked at regular weekly intervals with paroxysms of shivering, followed by fever and sweating. He was supposed at first to have a recurrence of an old intermittent fever, and later to have hepatic abscess; but at last his symptoms indicated and the necropsy proved that his actual and only disease was a gall-stone so impacted as to produce great irritation, but not complete obstruction of the common duct. Similar cases have been noticed by Charcot (8), who argued that the fever is due to the absorption of some poison into the blood. Dr. Murchison was of opinion that such attacks are not of a poisonous or septic origin, but are due to nervous irritation.

From the cases I have seen I should think that both explanations are admissible; the fever not being unlike that known as "urethral," in which the same contention as to causation arises. In a very interesting and important paper, Dr. Osler of Baltimore (28) says that the combination of the following symptoms is characteristic of the existence of gall-stones in the common duct, and is, therefore, valuable in distinguishing between that form of obstruction and malignant tumour:—

1. Jaundice of varying intensity, deepening after each paroxysm, which may persist for months or even years.
2. Ague-like paroxysms characterised by chill, sweating, and fever, after which the jaundice usually becomes more intense.
3. At the time of the paroxysm, pains in the region of the liver, with epigastric disturbance.

This is fully borne out by my experience, and in a number of cases of jaundice of several months' duration, where there was this combination of symptoms, I have operated and found gall-stones impacted in the common duct, and have succeeded in crushing them and passing on the fragments into the bowel.

In addition to the symptoms already mentioned, the following complications may be met with, and may constitute the prominent changes threatening life and requiring treatment; the original cause having perhaps disappeared, or being masked by more serious sequels:—(i.) Ileus, due to atony of the bowel, leading to enormous distension and to the symptoms and appearance of acute intestinal obstruction, apparently the consequence of the violent pain. (ii.) Acute intestinal obstruction dependent on: (*a*) paralysis of gut due to local peritonitis in the neighbourhood of the gall-bladder; (*b*) volvulus of small intestine; (*c*) impaction of a large gall-stone in some part of the intestine after ulcerating its way from the bile-channels into the bowel; (*d*) stricture of intestine or adventitious band originally produced by gall-stones. (iii.) General hæmorrhages, the result of long-continued jaundice, either dependent on gall-stones alone or on cholelithiasis associated with malignant disease. (iv.) Localised peritonitis producing adhesions, which may then become a source of trouble and pain, even after the gall-stones have been got rid of. I believe that nearly every serious attack of biliary colic is accompanied by adhesive peritonitis, as my experience is that adhesions are found in all cases where there have been characteristic seizures. (v.) Dilatation of stomach dependent on adhesions around the pylorus. (vi.) Ulceration of the bile passages establishing a fistula between them and the intestine. (vii.) Stricture of the cystic or common bile-duct. (viii.) Abscess of the liver. (ix.) Localised peritoneal abscess. (x.) Abscess in the abdominal walls. (xi.) Fistula at the umbilicus or elsewhere on the surface of the abdomen, discharging mucus, muco-pus, or bile. (xii.) Empyema of the gall-bladder. (xiii.) Suppurative cholangitis. (xiv.) Septicæmia or pyæmia. (xv.) Phlegmonous cholecystitis. (xvi.) Gangrene of the gall-bladder. (xvii.) Perforative peritonitis due to ulceration or to rupture of the gall-bladder or ducts. (xviii.) Extravasation of bile into the general peritoneal cavity. (xix.) Pyelitis of the right side. (xx.) Cancer of the gall-bladder or of the ducts. (xxi.) Subphrenic abscess. (xxii.) Empyema of the right pleura. (xxiii.) Pneumonia of the lower lobe on the right side (xxiv.) Chronic invalidism and inability to perform any of the ordinary business or social duties of life.

Diagnosis.—In the sections on Tumours of the Gall-bladder and on Inflammatory Affections of the Bile Passages the diagnosis of the complications of gall-stones is more fully dwelt upon; so that in this section it is only necessary to remark on the diagnosis of uncomplicated cholelithic attacks: under this heading we have to consider the several ailments which may produce painful seizures in the right side of the abdomen. These are:—(*α*) Hysteria or nervous spasms; (*β*) Acute dyspepsia with flatulency; (*γ*) Appendicular colic; (*δ*) Right renal colic; (*ε*) Spinal neuralgia; (*ζ*) Malignant growth in or near the liver; (*η*) Pyloric stenosis; (*θ*) Lead colic.

The diagnosis chiefly rests on paroxysmal attacks of pain, starting in the right hypochondrium, and radiating thence over the abdomen and through to the right scapula—the attacks being often accompanied by vomiting or collapse, and sometimes followed by jaundice, although jaundice is frequently absent. If jaundice be persistent, the presence of malignant disease may be suspected. If, however, the jaundice be dependent on gall-stones, ague-like attacks will probably be present.

Just as in appendicitis there is tenderness over M'Burney's point, so in gall-stones, with very few exceptions, marked tenderness will be found on pressing the finger deeply over the region of the gall-bladder, or over some point between the ninth costal cartilage and the umbilicus.

In several cases that I have seen, the pain in the so-called "spasms" has been referred to the left side, thence radiating to the left infrascapular region; and in operating on such cases I have found the pylorus adherent to the gall-bladder or cystic duct. In hysteria, the irregularity of the attacks, their association with other neurotic phenomena such as polyuria, globus hystericus, and so forth, together with the absence of collapse and of the physical signs of gall-stones, will enable us to arrive at a correct conclusion. In acute dyspepsia with flatulency, the relief following on simple treatment, the pain over the stomach rather than over the gall-bladder, the discovery of a manifest cause and the absence of serious symptoms distinguish so-called stomach "spasms" from gall-stone attacks. In appendicular colic, the almost universal signs of tenderness at a point midway between the anterior superior spine of the ilium and the umbilicus ("M'Burney's point"), the presence of a swelling in the right iliac fossa or near it, and the absence of right scapular pain, render the diagnosis of this condition free from serious difficulty, though in cases of phlegmonous cholecystitis with peritonitis the latter has sometimes been attributed to appendicitis instead of its actual cause. In right renal colic, the associated urinary symptoms, together with the character of the urine and the pain passing down the right genito-crural nerve into the testicle, are distinctive.

In lead colic, the more or less persistent "stomach ache," the absence of the usual gall-bladder paroxysms, and the presence of a blue line on the gums, will usually assist in the diagnosis; but if in doubt, the result of treatment by iodide of potassium and saline aperients will shortly clear it up.

In pyloric stenosis, if accompanied by adhesions around the pylorus, the symptoms are not unlike those of gall-stones, with which, in fact, the affection may be associated, as in several cases I related before the Clinical Society in 1893. The presence of dilated stomach, the characteristic vomit, the contraction of the stomach wall, the pain in the left of the abdomen, and the absence of the characteristic gall-bladder pain, will usually establish the diagnosis.

In spinal neuralgia, the presence of tenderness over the spine, the course of the pain along the branches of the corresponding spinal nerves, the presence of tenderness of the skin, and the absence of collapse and of vomiting put aside all difficulty.

In malignant disease, the absence of pain and tenderness, or, if pain be present, its continued character, the gradual and persistent loss of flesh, and the more marked failure of strength, usually indicate the serious nature of the affection. The persistence of jaundice when once it supervenes, the absence of ague-like attacks, and, if the disease involve the head of the pancreas, the almost constant presence of a tumour due to enlargement of the gall-bladder, afford landmarks which as a rule prove true guides; but in many cases gall-stones exist along with malignant disease, and then these symptoms become indeterminate, though the rapid wasting and loss of strength will often lead to a successful diagnosis of the co-existence of the two conditions. If nodules form in the liver, and if ascites with œdema of the feet supervene, the condition becomes manifest at once.

The so-called diagnostic operations of sounding for gall-stones, and aspiration of a distended gall-bladder, I believe to be futile and dangerous; a small exploratory incision is far better, whether for information or treatment.

The treatment of gall-stones may be considered under the headings —Preventive, Palliative, and Radical. The two former resolve themselves into medical, the latter into surgical treatment.

Medical treatment.— The preventive treatment of cholelithiasis is chiefly a matter of diet, exercise, and general hygienic surroundings. As women suffer from gall-stones much more frequently than men, it has been thought that their mode of dress, and especially the wearing of stays, may be one of the causes; but probably the want of sufficient exercise, with constipation and rich living, its frequent concomitants, are more to blame. In prescribing prophylactic measures one would recommend rational clothing (which of course includes the avoidance of tight lacing), temperance in diet, warm baths, fresh air and regular exercise. In regard to diet, more depends on temperance than on the choice or refusal of certain foods. In giving directions on diet patients may with advantage be told to avoid over-indulgence in sweet and starchy foods and in rich dishes, which tend to induce dyspepsia. Alcohol should only be taken in moderation, well diluted, and with food.

According to the views expressed in considering the cause of the formation of gall-stones, either a sufficiency of albuminous food in the shape of meats or game should be taken, or farinaceous foods which contain a fair proportion of nitrogen. If there be any benefit in the administration of olive oil, the use of butter or of animal fats, if taken in quantities short of producing dyspepsia, should have a similar effect.

Dr. Lauder Brunton gives some valuable hints on treatment, and shows how the system of dieting adopted at certain watering-places, when combined with exercise and the administration of diluent beverages (water being the essential element), has very beneficial results. I have been accustomed for some years to recommend patients suffering from cholelithiasis to drink a tumblerful of the natural Carlsbad water with a little hot water before breakfast, and a tumblerful of simple hot water before the later meals; for I think there can be no doubt that, as a rule, too little water is taken, and the inspissated or stagnant bile and mucous deposit, if not removed, will tend in the long run to form concretions; just as drains, if not flushed from time to time, will become blocked by the deposit of solid matter.

Alkaline saline waters (particularly the hot Carlsbad) act beneficially by stimulating the peristalsis of the digestive tract, and increasing the flow of blood to the abdominal organs. In the peristalsis the bile passages participate, and the movements of the bowels act as a form of massage, while the diseased mucous membrane benefits by the increased flow of blood. The injection into the rectum of large quantities of hot water serves the same purpose. When gall-stones have once formed, no medicine, so far as we know, can dissolve them or produce any material benefit except by way of palliation; and although numerous remedies have been vaunted as beneficial in the dissolution of gall-stones, their advocates have argued as if the gall-stones were in a test-tube; forgetting, apparently, that no drug can reach the concretions save by a circuitous route, and in an extremely diluted form: thus benzoic acid, benzoate of soda, salicylic acid, turpentine, ether, chloroform, and numerous other agents reputed to be beneficial, can really have no material effect. I would not for a moment say, however, that rational medical treatment may not restrict the increase of gall-stones already formed, or prevent the formation of new ones, and thus prove really curative, if the patient have the good fortune to part with those already formed.

The experiments of Dr. Brockbank (5) effectually dispose of the supposition that the so-called saline cholagogues have any solvent action on gall-stones; for after allowing concretions to stand in a 1 per cent solution of the various salts for fourteen days and then weighing them, he found that there had been no loss of weight. Among the drugs experimented on were the salicylate, the sulphate, the benzoate, the phosphate, the bicarbonate, and the chloride of soda; the sulphate of potash and the chloride of ammonium.

Similar experiments with olive oil, oleic acid, and a solution of sapo-animalis, yielded far different results. A gall-stone, placed in pure olive oil, in two days lost 68 per cent of its original weight, and then broke up into small pieces. With pure oleic acid a similar result followed in a much shorter space of time: a small gall-stone disappeared in twenty-four hours, and a larger one, after losing 63 per cent of its weight in two days, broke up into small fragments in four days. The effect of a solution of animal soap on the concretions is remarkable: after standing for a few hours in a 5 per cent solution, a gall-stone becomes coated with a bluish-white filmy material, and in time the solid matter becomes viscid. In view of the fact that the administration of olive oil is said to exert a curative effect in cholelithiasis, these experiments are interesting; but as there is not the slightest evidence that the oil can reach the gall-stone in the gall-bladder or cystic duct, there must be some other than direct solvent action to explain the beneficial effect; indeed, the effect itself is doubted by some observers, and requires more direct proof before it can be accepted. An explanation is offered in Dr. Brockbank's paper:—"Another explanation of the reported disappearance of the gall-stones after large doses of oil may be derived from the action of soap and fats on cholesterin. A digested fat passes into the circulation from the alimentary canal in three forms—as unchanged fat, and as the corresponding fatty acid and soap. All occur normally in the bile, and the amount present in the bile increases with the amount of fat taken in the diet. Oil, fatty acids, and soaps all dissolve cholesterin readily and break up a gall-stone. If, then, the oil, fatty acid and soap appear in the bile in increased amount after large doses of oil, it is very probable that the gall-stone is attacked by them, especially by the soap, and in time is dissolved, or so reduced in bulk as to be enabled to pass out into the duodenum."

I have tried olive oil in large doses in several cases, and cannot say that I have seen any good to result from its employment, unless it were in one case of impacted calculi in the common duct, on which I operated after the olive oil treatment had been tried for some weeks; I then found that the gall-stones yielded more readily than usual to the pressure of the finger and thumb, as if the treatment had lessened their consistency.

The oil may be administered either by the mouth or by the rectum; in either case from two to ten ounces should be given daily. It is not readily taken except with food, and then it is apt to excite dyspepsia.

Dr. Goodhart gives an account of five cases of probable cholelithiasis in which olive oil had been administered with apparent benefit. He remarks: "With reference to the results, I wish to say that it is obvious that I cannot claim for these cases anything more than a suspicion in favour of the value of the administration of oil. In no one of the cases have gall-stones been proved to have passed, and in none of the cases has the improvement been so immediate that effect and cause certainly go together." Dr. Kishkin's experiments apparently show how a mistaken idea of its benefit has arisen. The supposed calculi which were parted with were found to consist of oleic, palmitic, and margaric acids combined with lime; and similar concretions could be produced at any time by giving olive oil to any person suffering from scanty biliary secretion; no true gall-stones were ever found in the motions after the olive oil treatment.

Belladonna has been said to have a specific action in cholelithiasis; and I can conceive that if a small concretion were passing along the ducts, by its special action on involuntary muscular fibre, it might aid in its expulsion. But my own experience would lead me to disagree entirely with a medical writer who says that a pill containing a quarter of a grain of belladonna and a quarter of a grain of podophyllin resin is a remedy as nearly approaching a specific as it is possible to obtain.

Massage finds a strong advocate in Dr. George Harley, who says: "For without doubt, perseverance and opportunity will in the end enable them (the operators) to discover gall-bladders equally as readily as the trained fingers of the expert do, and that, too, even through abdominal parietes so thick that untrained hands cannot so much as make out the boundary of the solid liver through them. While, again, they will ultimately find that they will be able to extrude small impacted biliary concretions, be they in the shape of sand, gravel, or stones, from the bile-duct into the duodenum with as much safety and certainty as they can pass a catheter through a stricture into a human urinary bladder. At the same time, for the sake of the patient's welfare as well as their own reputation, they must never forget to be as careful in the mode of operative procedure in the one case as in the other, as neither operation is invariably unattended with danger. This is especially the case when the manipulative operation has been, unfortunately, delayed until the gall-stones have grown large and hard, and, on account of the prolonged pressure, begun to ulcerate through the tissues they have long pressed against."

It is scarcely necessary to do more than draw attention to the description of the gall-stones at the beginning of this chapter in order to point out how futile, nay more, how injurious massage must be in many cases, however skilfully performed; for not only is it unlikely, but in by far the greater number of cases it is utterly impossible that the concretions can be forced through passages as narrow as we know the cystic and common ducts to be.

Some little time ago I was called to a distance to operate on a patient who had been under this treatment judiciously and systematically carried out, and had nearly died under the process; so that I had to operate in a much more unfavourable condition than would otherwise have been the case. Fortunately, however, I was able to remove the gall-stones, and the patient is now well. I can only say that were I the subject of cholelithiasis I would not submit to massage, nor could I conscientiously recommend it; although it may possibly aid in the expulsion of small calculi, it is impossible to diagnose the absence of large ones, or to know the exact condition of the ducts which may possibly be ruptured by manipulation.

During a gall-stone attack, relief is urgently demanded; at times the drinking of a pint of water as hot as it can be taken, especially if combined with the application of hot fomentations over the region of the liver, will assuage the pain; at other times the administration of thirty drops of spiritus etheris in two teaspoonfuls of chloroform water every quarter of an hour will answer the same purpose. In some cases I have found exalgine, in one-grain doses, dissolved in a teaspoonful of hot water and repeated every half-hour for three or four doses, to prove of service.

In many cases, however, the only satisfactory remedy is a morphia injection.

Surgical treatment. — After medical treatment has been fairly and fully tried and failed, I think both physicians and surgeons are now agreed that surgical measures should be resorted to. While cholecystotomy is generally recognised as the operation to be aimed at in the treatment of affections of the gall-bladder or bile-ducts, especially in cholelithiasis, it is often impossible to say what operation will have to be done until the abdomen is opened.

The indications for operating would seem to me to be as follows:—

1. In frequently recurring biliary colic without jaundice, with or without enlargement of the gall-bladder.

2. In enlargement of the gall-bladder without jaundice, even if unaccompanied by great pain.

3. In persistent jaundice ushered in by pain, and where recurring pains, with or without ague-like paroxysms, render it probable that the cause is gall-stones in the common duct.

4. In empyema of the gall-bladder.

5. In peritonitis starting in the right hypochondrium.

6. In abscesses around the gall-bladder or bile-ducts, whether in the liver, under or over it.

7. In some cases where, although the gall-stones may have passed, adhesions remain and prove a source of pain and illness.

8. In fistula, mucous, muco-purulent or biliary.

9. In certain cases of jaundice, with distended gall-bladder dependent on some obstruction in the common duct. In such cases the increased risk must be borne in mind, as malignant disease may be the cause of the obstruction, and operation in such cases is attended with greater danger than ordinary.

10. In phlegmonous cholecystitis and in gangrene if the case be seen and recognised at a sufficiently early stage of the disease.

Supposing the case to be a suitable one for cholecystotomy, and the gall-bladder and ducts can be cleared without great difficulty by means of forceps within and the fingers outside the ducts, the opening in the gall-bladder can be sutured to the aponeurosis—which I think preferable to skin fixation—and so drained; this I infinitely prefer to immediate suture of the opening.

But if the ducts cannot be cleared, what may be done?

(*a*) Cholelithotrity, or crushing of the gall-stones in place by means of the finger and thumb, or by padded forceps; I have successfully performed this operation on many occasions, and I prefer it to the more formidable procedure of incising the ducts or of fixing the gall-bladder to the intestine.

(*b*) Choledochotomy, or incising the duct, whether cystic or common, the incision being afterwards sutured; this is no easy matter on account of the depth of the parts to be coapted; I have found the stitching to be best effected by means of a rectangular cleft-palate needle. A drainage-tube should always be inserted into the right kidney pouch in these cases; and if a transverse incision be made and the tube brought out through the lower end of this, the drainage is so efficient that even if the sutures fail to close the wound in the duct there will be little fear of extravasation.

(*c*) Cholecystenterostomy, or the making of an anastomosis between the gall-bladder and intestine, is easily effected if the gall-bladder be dilated, but with difficulty if the gall-bladder be contracted, as often is the case. I have performed this operation six times, with immediate success and recovery in all, and with complete and permanent cure in five. My decalcified-bone bobbin enabled me to accomplish the anastomosis rapidly. However, I used "Murphy's button" in my last three cases, and in future I shall always employ it in such cases, as being a more speedy method.

(*d*) The daily injection of fluids, after an interval of some days, through the cholecystotomy opening, which will either soften or dissolve the concretions. For this I have used hot water, ether, and ether and turpentine with more or less success; but I think Dr. Brockbank's suggestion to use an injection of olive oil, or of oleic acid, or a 0·5 per cent solution of sapo-animalis, is worth a fuller trial.

(*e*) Cholecystectomy, or excision of the gall-bladder, can seldom be advisable or necessary as a primary operation in gall-stones, and extremely rarely possible in malignant disease. It may be required as a secondary operation in cases of stricture of the cystic duct, the common duct being free. On three occasions in which I have excised the gall-bladder it was for mucous fistula depending on stricture of the cystic duct following on gall-stones, and all the patients were completely and permanently cured.

In cholecystotomy, where it is impossible to bring the margins of the incised gall-bladder into the wound, and where the parietal peritoneum cannot be tucked down to meet the edges of the opening, I have made a tube of the omentum; but in such cases no hesitation need be felt in trusting to a drainage-tube, as the peritoneal cavity soon becomes occluded around the drain, and there is little or no tendency for the bile to pass among the viscera; a suprapubic drainage opening, therefore, is quite unnecessary.

The combined button and drainage-tube suggested by Dr. Murphy may prove useful in some cases of this kind; but as the gall-bladder is usually shrunken, I suspect it will be of service in exceptional cases only. With very few exceptions, I have found a vertical incision along the upper part of the right linea semilunaris to give ample room, but if required I have not hesitated to get further room by a transverse cut in addition.

Suture of peritoneum, aponeurosis, and skin by separate stitches effectually guards against ventral hernia, if the patient be kept recumbent for from twenty-one to twenty-eight days; and if a firm oval pad be worn under a belt for a few months subsequently. In all cases strict antiseptic precautions should be observed, and the abdomen must be left as clean and dry as possible.

In conclusion, I would emphasise that with due skill and adequate care, operations on the gall-bladder and bile-ducts are among the most successful of the major operations; but as many of them are extremely difficult, and as it is impossible to say beforehand whether any case may not prove so, I think such surgical work should be undertaken only by those who have had experience in abdominal surgery, and who have witnessed or helped in several operations of this kind. As soon as this rule is understood we shall cease to witness the varying rates of mortality in the hands of different operators—from 50 to almost 0 per cent—and we shall probably find that, excluding cases of malignant disease associated with jaundice, the all-round mortality will not exceed 5 per cent. I hope the time is not far distant when it will be fully recognised that though cholelithiasis, so far as its causes and its early treatment are concerned, is distinctly a condition for medical treatment, it is both unjust to the patient and unfair to the profession to continue medical treatment and to postpone surgical aid until serious complications supervene, or the patient is almost, if not quite past relief.

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REFERENCES

1. Barbacci. *Medical and Surgical Reports*, June 1, 1889.—2. Biggs, G. P. *New York Hospital Gazette*, 1895.—3. Birch, De Burgh. *Journal of Physiology*, No. vii.—4. Brockbank, E. M. *On Gall-stones.* London, 1896.—5. *Idem. Medical Chronicle*, November and December 1893.—6. Brunton, Lauder. Goulstonian Lectures, *Brit. Med. Journ.* 20th June 1891.—7. Chadwick *Brit. Med. Journ.* Jan. 1895, p. 1143.—8. Charcot. *Maladies du Foie*, 1877.—9. Charcot and Gombault. *Arch. de physiol. et path.* 1876.—10. Courvoisier. *Casuistisch-Stat. Beitrage z. Path. u. Chir. d. Gallenwege.* Basel, 1890.—11. Donkin, H. B. *Lancet*, Jan. 5, 1895, p. 28—12. Escherich. *Fortschritt der Medecin*, 1885.—13. Fenger. *Amer. Jour. of Med. Sciences*, Feb. 1896.—14. Gilbert and Dominici. *Compt. rend. Soc. Biol.* Dec. 23, 1893.—15. Gilbert and Girode. *Ibid.* 1890, No. 39.—16. *Ibid.* Dec. 2, 1893.—17. Goodhart. *Brit Med. Journ.* 30th Jan. 1892.—18. Harley, G. *Medical Annual for* 1890.—19. Hotchkiss, L. W. *Annals of Surgery*, Feb. 1894.—20. Lake. *Lancet*, March 1894.—21. Lane, W. A *Lancet*, Feb. 25, 1893.—22 Lockwood, C. B. *Lancet*, March 2, 1895.—23. Musser. *Boston Med. and Surg. Journ.* Oct. 15, 1889—24 Naunyn. *Klin der Cholelithiasis*, 1892.—25. Netter *Progrès médical*, 1886.—26. Norton, C. A. *Lancet*, 1893.—27. Ord. *Address to Brit. Med. Assoc.* 1887.—28. Osler *Principles and Practice of Medicine.*—29. *Idem.* "Symptoms of Chronic Obstruction of the Common Bile-duct by Gall-stones," *Annals of Surgery*, March 1890.—30. Potain. *Journ. de méd. et chir.* Nov. 1882.—31. Robson, A. W. M. *Proc. Royal Soc.* vol. xlvii.—32. Rolleston. *Med. Chronicle*, Jan. 1896.—33. Schroeder. Statistics quoted in Dr. Brockbank's paper.—34. Swain. *Lancet*, Mar. 24, 1895.—35. *Idem. Lancet*, March 23, 1895.—36. Terrier. *Brit. Med. Journ.* 1894.—37. Thudichum. *Treatise on Gall-stones*, 1863.—38. White, Dr. Hale. *Path. Soc. Trans.* vol. xiii.—39. Willards. *Trans. Amer. Med. Assoc.* 1893.—40. Williams and Sheild. *Lancet*, March 2, 1895

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CHOLANGITIS

INFECTIVE CHOLANGITIS, or infective catarrh of the bile-ducts, is usually due to gall-stones in the common duct, which favour the entrance of organisms from the intestine through the duodenal orifice.

Courvoisier, Osler, and Fenger have each described the ball-valve action of gall-stones in a dilated common bile-duct or in the ampulla of Vater; thus accounting for the intermittent character of the jaundice and the irregular course of the disease.

Charcot was one of the first to describe the disease under the name of *intermittent hepatic fever.*

I have operated on a considerable number of cases of infective cholangitis dependent on gall-stones in the common duct, but although on several occasions the gall-stones were freely movable or even floating, in by far the greater number they were multiple and more or less impacted.

The usual history is one of spasms for several years without jaundice; then comes a more severe seizure followed by temporary icterus. If the gall-stone pass, there is an end of the trouble; if not, the next attack of pain is probably followed at once by a shiver and by all the symptoms of an "ague fit," the temperature frequently reaching 104° or 105°. After it has passed off, the skin is more deeply tinged and the jaundice may persist, though inconstant in degree; it rarely, however, disappears completely between the attacks; there is usually a slight icteric tinge of the conjunctivæ, even though the interval between the attacks may be one of weeks or months. The rigors may be repeated daily or at irregular intervals.

The gall-bladder may be felt as an enlargement below the right costal margin, but this is not usual, as if gall-stones be present it is more common to find the gall-bladder contracted. The liver at first is not enlarged, but later it may descend considerably. Tenderness over the gall-bladder or in the epigastric region can generally be elicited. There is usually well-marked loss of flesh and strength; and, if unrelieved by nature or art, the disease may run on into suppurative cholangitis and its complications.

Infective cholangitis may persist off and on for years, and may lead to recovery; on the other hand, it may assume an acute form and lead to death from pain, biliary toxæmia and exhaustion. The complications which may follow are diffuse hepatitis, abscess of the liver, cholecystitis and empyema of the gall-bladder, perforation of the ducts, endocarditis, pleurisy, pneumonia, and other septic diseases.

Diagnosis.—Ague, being now a rare disease in England, is not so readily assumed as it is in countries where malaria is endemic, though the regularity of the chills and the slight jaundice and enlargement of the *spleen in some cases may suggest it; yet the pain and tenderness, the* history of cholelithiasis, and the failure of relief by large doses of quinine, soon settle any doubts.

As infective diseases in the bile passages are prone to end in suppuration, abscess of the liver and suppurative cholangitis may supervene; but the more prolonged course of infective cholangitis, the comparative good health between the attacks, the irregularity in the course of the disease, and the absence of rapid and progressive deterioration of health will usually enable a diagnosis to be made.

When suppuration exists we usually find increased tenderness over the liver area, continued or irregular intermittent fever, and intense and persistent jaundice.

Treatment.—If possible the cause should be removed, but, should this prove impossible, the ducts can be drained; fortunately this may be accomplished with every prospect of success, if, as is commonly the case, the primary disease be gall-stones. For instance, I have operated on two hundred cases of disease of the gall-bladder and bile-ducts, and in no case where gall-stones were unaccompanied by malignant disease or by suppurative cholangitis have I lost a patient; even if I include all the complicated cases, the rate of recovery is still 96 per cent. Indeed, there can be no doubt in the minds of those who have observed many of these cases that it is better to anticipate the complications; and that as soon as medical treatment has been fairly tried and failed, the removal of gall-stones by surgical means should be resorted to.

SUPPURATIVE CHOLANGITIS of the bile-ducts is a subject of considerable interest both to the physician and surgeon. Its gravity lies not only in its causation, but in the combined effects of biliary obstruction with septic infection, and their local and constitutional effects also.

Etiology.—The most frequent cause is gall-stones, and of this series the museums furnish many examples. One in Guy's Museum shows the ducts throughout the liver inflamed, dilated, and associated with several small abscess cavities; the cause being a gall-stone floating in the common duct. The parts were taken from a woman, aged thirty, who had had enteric fever five months before death; the death was due to pyrexia accompanied by rigors.

But, besides gall-stones, hydatid disease, cancer of the bile-ducts, typhoid fever, and influenza may cause suppurative cholangitis; and I suspect that the disease not infrequently accompanies other acute infectious ailments.

There are good examples of cholangitis due to hydatid disease in St. Bartholomew's, Guy's, St. George's, and the Middlesex Museums; so that it is evidently no infrequent cause. In some of these instances a hydatid cyst has burst into a bile-duct, and in several of these a piece of rolled-up hydatid membrane projects through the papilla into the duodenum. In all these cases the ducts throughout the liver are dilated and filled with pus.

Some years ago I operated on a case of suppurative cholangitis dependent on malignant disease in the common duct. The patient was decidedly relieved for a time by the drainage established by cholecystotomy; he ultimately died, however, from the original disease, and at the autopsy the whole of the ducts throughout the liver were filled with muco-pus.

A very good example of suppurative cholangitis arising as the result of cancer of the ampulla of Vater may be seen in St. Thomas's Museum.

In typhoid fever the disease arises irrespective of any organic obstruction in the ducts, as is shown by a specimen of Dr. Hale White's in Guy's Museum, where death occurred in the seventh week of typhoid; there was inflammation of the bile passages within and outside the liver, together with cholecystitis.

I do not think that influenza has been noted as a cause of suppurative cholangitis. I observed the connection some time ago; and the symptoms were so characteristic, and came on, in a lady of sixty-two, within so short a time of influenza, that I think there is every reason to believe this infection to have been the origin of the suppuration.

The aforementioned diseases are somewhat remote terms in the series of causation; the immediate cause is the presence of pyogenetic organisms within the biliary passages.

Symptoms.—In suppurative cholangitis there is usually progressive enlargement of the whole liver, which may descend as low as the umbilicus; the swelling being uniform, smooth, and tender to pressure. If the cause be in the common duct, and the gall-bladder has not previously become contracted, there will be the additional enlargement caused by its distension; but when contraction of the gall-bladder has taken place, and also when the obstruction is in the hepatic duct, there will be no signs of cholecystitis.

Pain may be entirely absent, as in one case on which I operated, where the disease was dependent on cancer of the common duct; but when the cause is gall-stones, as in many cases that I have seen and in some on which I have operated, the pain is severe and paroxysmal, each attack being accompanied by ague-like seizures and an intensification of the jaundice. Jaundice is always present, and is usually both persistent and intense; though where the obstruction is a floating gall-stone, acting like a ball-valve in the common duct, the jaundice may vary from time to time, or may almost disappear. Fever, with occasional rigors and profuse perspiration, is a prominent feature of the disease, and rapid loss of flesh and strength likewise. The disease is always serious, and often proves fatal; though, if the cause can be removed at an early stage, recovery may occur.

If the course be subacute the inflammation may concentrate itself in some part of the liver and lead to abscess; in this case a distinct tender swelling may form and give rise to the usual symptoms and signs of hepatic abscess. If ordinary infective cholangitis pass on to general suppurative cholangitis recovery is improbable.

Hepatitis and multiple liver abscesses frequently follow cholangitis, and are usually followed by general and fatal infection of the system.

Pneumonia and pleurisy ending in empyema are serious and not infrequent complications.

Endocarditis at times occurs, and as it has been known to follow cholangitis without hepatitis, and cholangitis without abscess, this cause should never be lost sight of in any case of infective endocarditis.

In these cases the bacillus in the vegetations on the inflamed endocardium has been found to be identical with that discovered in the infected bile.

Jaccoud and Aubert have also found endocarditis in cases of cholangitis.

Treatment.—Unless free evacuation of the infected contents of the bile passages can be accomplished, either naturally or artificially, treatment is virtually useless. If practicable, cholecystotomy should therefore be performed, and free drainage established and continued until the bile is sterile, or nearly so. Although good results cannot be expected in all cases, an amelioration of the symptoms may be looked for in a fair proportion, and complete relief in others.

If a localised abscess be discovered in the liver, it should be opened and drained, and though in these serious cases it is scarcely to be expected that operation can be always successful, the chance of permanent benefit is worth snatching at, even under the most desperate conditions. Of general means, warm applications to the hepatic regions, an initial mercurial purge followed by milder saline laxations, intestinal antisepsis by bismuth and salol, the relief of pain by sedatives if called for, and the treatment of symptoms as they arise, will afford some amelioration, though the relief will probably be but temporary.

Surgeons have been performing cholecystotomy for infective cholangitis for some years (for instance, my first operations for cholecystitis and cholangitis occurred so far back as 1888); yet I think it is just to give the chief credit of specially pointing out the great importance of surgical treatment in cholangitis to M. Terrier.

On the opening of the gall-bladder a certain number of important therapeutic results follow.

1st, The septic contents of the gall-bladder are evacuated. 2nd, Calculi, which are most frequently present there, are removed. 3rd, The other biliary passages, more or less obstructed either by calculi or by swelling of their walls, are rendered as free as possible. 4th, The septic bile is allowed to escape and mechanically washes out the lower passages, carrying away through the drainage-tube many of the infectious elements. 5th, The relief of pressure prevents absorption of the septic elements. 6th, The relief to the kidneys, by allowing the bile to escape freely, is also of importance; as they are thus enabled to perform their function more freely in relieving the system of septic and other materials.

In the paper referred to, M. Terrier narrates several cases in the utmost detail, an account especially interesting, as he describes the bacteriological examination of the discharge from the fistula at different dates, and conclusively shows the gradual diminution in the virulence of the discharge after some days' drainage, and points to the need of rather more prolonged drainage than some of us have been wont to employ; until, indeed, the bacteriological examination of the discharge shows it to be sterile, or nearly so.

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REFERENCES

1. CHARCOT. *Maladies du Foie*, 1877.—2. JACCOUD and AUBERT. *Clin. méd. de Lariboisière.*—3. NETTER and MARTHA. *Arch. de physiol.* vol. ix. 1886.—4. ORD. *Brit. Med. Journ.* Aug. 1887.—5. OSLER. *Annals of Surgery*, 1890.—6. ROBSON, MAYO. *On Gall-Stones*, 1892.—7. TERRIER. *Rev. de chir.* 1895, p. 966.

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CONGENITAL OBLITERATION OF THE BILE-DUCTS

Description.—Under the heading of "Congenital Obliteration of the Bile-ducts" may be described a series of cases of infantile jaundice in which there is a progressive inflammatory condition of the bile-ducts and gall-bladder. The morbid process originates in intra-uterine life from an unknown cause, leads generally to complete obliteration of the lumen of the affected parts accompanied by biliary cirrhosis of the liver, and always ends in early death.

The disease is a comparatively rare one, but some sixty or seventy cases authenticated by post-mortem examinations have been put on record. It presents features of considerable interest, not only on account of the obscurity of its causation, but also because it represents, as it were, one of Nature's attempts at "experimental pathology."

Clinical features.—The parents of the patients seem generally to have been healthy people, and yet, in a considerable proportion of the cases, it is found that they have previously had one or more infants similarly affected. Instances are on record where as many as seven or even ten cases of infantile jaundice, apparently of this nature, have occurred in one family. Boys are affected about twice as often as girls.

At birth the child appears normal and well nourished, and nothing attracts special attention to it until either the whiteness of the stools or the yellow discoloration of the skin is noticed.

The jaundice is always a very marked feature, but the date of its onset varies considerably. Sometimes it is present at birth, often it is not noticed until the second or third day of life, occasionally it does not set in until the ninth, tenth, or even fourteenth day. When first observed the yellow colour is slight in degree, but within a day or two it noticeably *deepens, and soon becomes of a dark greenish-yellow hue. It remains until death; it may, however, vary a little in intensity from day to day,* and, if the child live for some time, the tint is often paler during the last few weeks.

It is to be observed that in those cases where only one of the hepatic ducts is obliterated, and also in those where all the ducts seem pervious, the jaundice may be just as severe as where the common duct is completely obstructed.

In some cases a quantity of dark, apparently normal meconium is passed in the usual way, and is followed at once by colourless motions; in others the fæces are devoid of colour from the very first. Rarely are any yellow fæces passed, but after a dose of mercury the stools may be partially greenish for a time. The bowels are generally costive. The urine is deeply bile-stained.

The occurrence of spontaneous hæmorrhages in various situations is a very characteristic symptom. A considerable number of the children suffer from bleeding at the navel, a symptom which usually sets in shortly after the separation of the cord (fifth to ninth day). It is of the nature of a general oozing from the raw surface, and is exceedingly difficult to stop; indeed it almost invariably results in death within two or three days at the farthest. Of those patients who survive the first fortnight a large number suffer from spontaneous bleeding from other parts, such as subcutaneous ecchymoses or epistaxis; or the blood may be vomited, or passed with the motions.

If the children are not carried off by hæmorrhage or some other such cause during the first week or two, they generally live from three to eight months. It is interesting, however, to observe that in those instances in which more than one child in a family was affected the tendency to hæmorrhage is particularly strong, and the patient scarcely ever survives the first fortnight.

Towards the end of the case there is more or less emaciation; but the interference with the general nutrition is usually much less than might be expected from the gravity of the lesion. Fits not infrequently come on, and, in the exhaustion of approaching death, some intercurrent disease, perhaps of a trifling kind, brings life to a yet earlier close.

Morbid anatomy.—The degree of the lesion affecting the bile-ducts and the gall-bladder varies to a very large extent in different cases. In a few, where the patient has not lived more than a week or two, no disease may be visible to the naked eye, and no evident obstruction to the outflow of bile may be discovered; in others the walls of the ducts are markedly thickened here and there. In most cases, however, some portion of one or other of the ducts or of the gall-bladder has its lumen completely obliterated, and the fibrous tissue round it is greatly increased in amount. Not infrequently parts of the affected structures have disappeared entirely, so that after death there is not even a strand of fibrous tissue to be found in their place. Extreme defects of this kind are most frequently found in cases where the patient has lived for *months*; but sometimes this is the state even at birth.

The exact site of the obliteration, when present, also varies indefinitely, there seems to be no place more apt to be affected than another.

The contents of the gall-bladder and ducts are by no means constant. If the child have lived more than a month it is usual to find colourless mucus only in the gall-bladder. Where coloured bile is present it is often described as unusually thick; and in one case (Campbell) the common duct was found blocked by an indurated cord-like plug of inspissated bile. In at least one instance (Bouisson) a gall-stone was found; and it seems quite possible that most, if not all, of the very rare cases in which gall-stones have been reported (18) in young infants may be examples of this disease.

Reports of microscopic examinations of the affected parts and the tissues in their neighbourhood are much wanted. In one case (23), where the lumen of the gall-bladder was almost totally destroyed, its walls were found enormously thickened and infiltrated with round cells, so as to look like granulation tissue. What remained of the cavity, however, was lined with cylindrical epithelium of normal appearance.

The blood-vessels of the liver are normal in uncomplicated cases.

The liver itself, when the child has lived for any length of time, is generally but not always enlarged. It is very tough in consistence, slightly uneven on the surface, and of a dark olive-green colour; on section it shows fine bands of fibrous tissue forming a network through it. Under the microscope the size and consistence of the organ are found to be due to the presence of typical biliary cirrhosis, and the green colour to innumerable small plugs of inspissated bile which distend the lesser ducts in many places up to their farthest ramifications; they may even seem to occupy minute cavities within the liver-cells.

The spleen is usually much enlarged.

The peritoneum, in most cases, is quite free from traces of disease, either past or present; but occasionally ascites or purulent peritonitis has been found. In a few of the reported cases there were adhesions in the neighbourhood of the ducts implicating the blood-vessels; in almost all of these there was good reason to suspect the presence of syphilis.

Nature and progress of the disease.—The nature of the lesions of the gall-bladder and ducts is such as to indicate that they must be the result of chronic progressive inflammation affecting the walls of these structures in a considerable extent of their course.

When this morbid process begins we cannot say; but certainly the period at which complete obstruction to the passage of bile occurs varies very greatly. In those cases in which no coloured meconium is passed it seems as if the ducts must have been blocked not later than the third month of intra-uterine life; while in others, where the amount of ordinary meconium is normal, the obstruction cannot have taken place until a very much later period.

The inflammatory lesions follow the course of the bile so closely that we can scarcely avoid the conclusion that they are secondary to some irritating change in the character of this fluid. That inspissated bile and gall-stones should have been found is, therefore, of importance. The frequent occurrence of complete stoppage of the passage of bile before there is any absolute anatomical blocking of the lumen of the ducts is also worthy of note, and suggests the possibility of a descending catarrh from irritating bile, such as is said to occur in poisoning by toluylendiamin and other substances (Stadelmann, Hunter).

Probably by the time that the infant is born the disease is always pretty far advanced. After birth the inflammatory process continues to spread, and leads to extensive obliteration and deformity; just as it sometimes does in adults when there is an impacted gall-stone (Courvoisier). The longer the child lives the more advanced, as a rule, is the deformity which is met with after death.

When the disease has gone on far enough to cause interference with the free passage of bile from the liver, biliary cirrhosis begins, as it does in the livers of animals whose common duct has been tied (Charcot and Gombault); and the amount of glycogen is diminished (Legg). This results in an increasing interference with those important functions of the liver by virtue of which it protects the organism from the dangers of auto-infection (Roger). To a sort of chronic blood-poisoning are due such symptoms as the vomiting, spontaneous hæmorrhages, and convulsions; and it gradually leads to emaciation, diminished vitality and death.

Etiology.—The causation of the disease is still most obscure. It seems certain, however, that congenital syphilis is not an essential element, although this has often been alleged. We learn from a study of the published cases that—(i.) Evidence of syphilis in the parents has very rarely been obtained—not in a tenth of the cases; (ii.) The brothers and sisters of the patients seem never to have shown signs of it; (iii.) In twenty-three cases, where the infants lived to be three months old and upwards, only twice were there noticed any of the symptoms which are usually attributed to congenital syphilis; (iv.) Ordinary syphilitic lesions have scarcely ever been found post-mortem in patients who have died of this disease. As already mentioned, however, it is just possible that the presence of this taint may promote the farther extension of the disease.

Severe digestive disturbances have been noted in the parents in several cases; and have been regarded as perhaps of etiological importance (Binz, Glaister).

The very remarkable fact that the disease so frequently occurs in several members of one family is one which must be taken into account in any theory of its etiology. This, and the very early period at which the morbid process begins, have led to its being attributed to an arrest of development. Nothing definite, however, can be said in support of this opinion.

The **diagnosis** may present some difficulty at first; but within a few days the deepening jaundice, colourless motions, and bile-stained urine render it evident that there is something more serious the matter than ordinary icterus neonatorum. Moreover, the comparatively slight effect produced at first upon the child's general health readily distinguishes these cases of jaundice from those associated with umbilical phlebitis and like septic conditions.

As the child grows older the occurrence of spontaneous hæmorrhages and the gradual enlargement of the liver and spleen strongly confirm the diagnosis.

The **prognosis** is, of course, of the utmost gravity ; no child proved to have this complaint has ever lived eight months. It should be mentioned, however, that a few cases of infantile jaundice have been reported as ending in recovery which, from their symptoms, and from their occurring in the same families as other children with obliterated bile-ducts, seem possibly to have been cases of this disease (Anderson, Freund, Grandidier)

Treatment.—Our ignorance of the causation of the disease, and the fact that it begins during intra-uterine life, put curative treatment out of the question in the only stage at which it could possibly be of any avail In a recent case (Giese) the abdomen was opened during life in the hope that, if the obstruction were situated low down, it might be possible to re-establish communication between the bile-channels and the intestine. This was not found practicable ; and the pathology of the disease certainly gives us little encouragement to expect even temporary relief from any surgical procedure.

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REFERENCES

1. Anderson. *Boston Med. and Surg Journ* 1850, Jan 2, p. 410 2 Binz. *Virchow's Archiv*, xxxv. S 360.—3 Bouisson *De la bile, de ses variétés, etc.* Montpellier, 1843 —4. Campbell, A. D. *Northern Journ. of Med.* Aug. 1844, p. 237. –5. Charcot and Gombault *Arch de physiol.* iii 1876, p 273 6 Cheyne. *Diseases of Children*, vol. ii p. 8 —7. Courvoisier *Casuistisch-Statistische Beitrage z. Path und Chirurg d. Gallenwege.* Basel, 1890.– 8. Freund. *Jahrb. f. Kinderheilk* ix. 1876, S. 178 9. Giessner *Ueber congenitalen Verschluss der grossen Gallengange*, Diss. Halle, 1886 –10. Giese. *Jahrb. f. Kinderheilk* xliii. 1896, S 252. 11. Glaister *Lancet*, 1879, i p. 293 —12. Grandidier. *Journal f Kinderkrankheiten*, May 1859, S. 380 —13. Henoch. *Lectures on Children's Diseases*, New Sydenham Soc. Transl. vol. i. p. 28.

14. Hunter, W. *Journ. of Path and Bacteriol.* July 1895, p. 264. –15. Legg, Wickham. *Bile, Jaundice, and Bilious Diseases*, 1880, p 641.—16. *Idem. St. Bart. Hosp. Rep.* 1873, ix. p. 178 – 17. Lotzi. *Berlin. klin. Wochenschr.* 1876, No. 30, S 438.—18 Mercat. "De la colique hépatique chez l'enfant," *These de Paris*, 1881. 19 Rogle. *Gaz. des hôp.* 1887, No. 66, p. 525.—20 Smith, Eustace. *Disease in Children*, 3rd edit. p. 718.—21. Stadelmann *Der Icterus*, Stuttgart, 1891, S. 260. —22. Thomson, John. *Edin. Med. Journal*, Dec. 1891, and Jan. and Feb 1892 ; this paper gives an almost complete list of previous cases.—23. *Idem. Edin. Med Journ* June 1892.—24. Underwood. *Diseases of Children*, 5th edit. vol i. p. 29.—25 West. *Diseases of Infancy and Childhood*, 8th edit. p. 718.

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ICTERUS NEONATORUM

Synonyms.—Normal, physiological, or idiopathic jaundice of new-born children.

Description. — Icterus neonatorum is a mild transitory form of jaundice of unknown etiology, which appears soon after birth in a large proportion of children otherwise normal, and passes off without subsequent ill effects.

Clinical features.—The disorder is an extremely common one, being met with, in a more or less marked degree, in a very large number of new-born children. Thus, Runge states the proportion of infants affected in this way as 80 per cent, Porak as 79-90 per cent, and Bouchut at 80-90 per cent. Probably the lowest proportion given is that of Holt, who reports that of 900 children born in the Sloane Maternity Hospital in New York, 300 were icteric.

It seems to be a matter of general experience that this discoloration is more frequently observed in hospital than in private practice. This has been attributed to the weakliness of hospital infants; but this may be but an apparent prevalence due to the good light more uniformly obtainable in institutions than in the bed-rooms of private houses. Certainly, however, it is more common in weakly infants with atelectasis, and in those that are born prematurely. The presentation at birth, the duration of the labour and its character—whether natural or artificial—are said to have no influence upon its production (Holt); and it is doubtful whether one sex is more affected than the other.

The yellowness of the surface of the body is generally the only discoverable symptom; the children in all other respects being perfectly well.

The icteric tint is usually seen for the first time on the second or third day of life, or a day or two later. It increases in depth for one or two days and then slowly disappears. In slight cases it may be quite gone in three or four days; often it lasts a week or more; but rarely, and in very severe cases only, does it persist for more than a fortnight. The degree of the discoloration varies from the slightest perceptible tinge to a deep yellow. When extremely slight it is best detected by pressing the point of the finger on the infant's red skin, and looking for a yellow tinge on the pale spot which the pressure produces.

The distribution of the jaundice and the order of its appearance are somewhat peculiar. First, and most distinctly, it is seen on the skin of the face—especially on the forehead and round about the mouth—and on the chest; later it appears on the sclerotics, and last of all on the hands and feet. Compared with the skin, the sclerotics are usually but slightly affected, and sometimes they remain quite normal in appearance. The slight and late implication of the eyes in these cases is an interesting point, as in ordinary obstructive jaundice the sclerotics are usually among the parts first and most deeply affected. The peculiarity is perhaps better expressed by saying that the skin in this form of jaundice is particularly early and particularly deeply tinged. This makes the degree of the jaundice appear much greater than it really is; this is to be attributed to the fact that the new-born infant's skin is especially hyperæmic (Cruse).

The urine, in most cases, appears quite normal, and does not leave a yellow stain on the child's napkins. In severe cases, however, bile pigment is present in it to such an extent as to discolour it. Parrot and Robin found little amorphous irregular masses of yellow pigment, sometimes floating free in the urine, sometimes embedded in epithelial cells and tube-casts. It seems that bile acids, although present in other fluids of the body, have never been demonstrated in the urine. According to Hofmeier, uric acid and urea are excreted in larger amount than by non-icteric children.

The fæces are normal in colour and in other respects. They are never decolorised as in ordinary obstructive jaundice.

Morbid anatomy.—Nearly all the internal organs show a yellow tinge, and this is true even of such tissues as the cartilages, brain, and spinal cord, which in adult jaundice are not generally discoloured. The tinge, however, is but slightly marked in the spleen and kidneys, and in the liver it is rarely discernible to the naked eye even in the most severe cases. The intima of the arteries, the endocardium, and other serous membranes, and also the serous fluids are deeply stained. The pericardial fluid contains not only bile pigment but bile acids also, as Birch-Hirschfeld, Hofmeister, and Halberstam have demonstrated.

The bile-ducts are normally formed and pervious; and apart from the general bile-staining of the tissues, no abnormality of any of the organs is discovered. In the necropsies which have been recorded, however, the condition of the ductus venosus, as to patency, does not seem to have received the attention it deserves.

Etiology.—A very large number of hypotheses have from time to time been propounded by eminent pathologists to account for this malady. Many of these have turned out to be baseless assumptions; others are still put forward as satisfactory explanations of the phenomena. None of them, however, has yet found adequate verification.

That bile acids as well as bile pigment are found in the pericardial fluid of icteric new-born children, and not in that of others, proves conclusively that the yellow colouring matter is really bile and comes from the liver. This effectually disposes of some of the older views, according to which this condition was a purely hæmatogenous form of jaundice, or even no jaundice at all, but merely a kind of local discoloration due to the red of the hyperæmic skin turning yellow as a bruise does in the process of fading Soon after birth very radical changes take place in the child's digestive organs and in its blood; these changes make it probable that at this time of life an especially large secretion of highly pigmented bile may occur as a physiological phenomenon. Yet how does this bile finds its way into the general circulation ?

The most important of the hypotheses which have been proposed to explain this problem may be summarised (Runge) as follows:—

i. A large number of observers have supposed that the hindrance to the outflow of bile lies in the bile-ducts themselves. Thus Virchow thought that plugs of mucus, which he found in the common duct, were the main cause of the jaundice; and Cruse and Epstein assumed that the circulatory changes occurring at birth induced hyperæmia and catarrh of the bile-ducts, with blocking from the desquamation of their epithelium. Kehrer, again, suggested that the bile-ducts must be the seat of positive congenital narrowing; and Cohnheim, that the bile was so much increased that the normal ducts became inadequate for its free escape for the time being.

ii. Others have attributed the supposed arrest of the flow through the bile-ducts to pressure on them from without by neighbouring blood-vessels. Weber thought that in the course of the ordinary circulatory changes following birth, the portal and hepatic veins might become so distended as to exert pressure on the ducts. Birch-Hirschfeld supposed that during or after birth the area supplied by the umbilical and portal veins becomes engorged, and that this leads to œdema of the connective tissue of Glisson's capsule, and thus to compression of the ducts. Silbermann drew attention to the destruction of coloured blood-corpuscles observed by him and Hofmeier in new-born children. He pointed out that where blood-dissolving processes go on there must be an increase in the fibrin ferment in the blood; so that the infant gets into a state of slight "fermentæmia," as he barbarously calls it. This would give rise to stasis and thrombosis in the portal system, resulting in compression of the bile-ducts and consequent reabsorption of the stagnant richly-coloured bile.

iii. Another group of authors, of whom Frerichs is the most prominent, say that the reabsorption of bile is due to a lowering of the blood-pressure in the capillaries of the liver tissue following on the closure of the umbilical vein.

iv. In 1885, Quincke proposed a very ingenious explanation which differs materially from those formerly suggested, and has not yet been disproved. He supposes that, in children with icterus neonatorum, the ductus venosus, which closes normally between the second and fifth days of life, remains open unusually late, and that this constitutes the essential cause of the jaundice. The blood of the portal vein usually contains a certain amount of the bile which has been reabsorbed into it from the bowel, and which it is carrying back to the liver. If, however, the ductus venosus remains open, it follows that part of this bile-containing blood will pass aside through it into the vena cava, and hence into the general circulation of the body. Although this suggestion stands in need of further anatomical confirmation, it may be mentioned that in one jaundiced infant of eleven days Ashby found the ductus venosus large enough to admit a director.

The **diagnosis** in uncomplicated cases presents no difficulty. The absence of serious symptoms, the slight degree of the jaundice, the pale urine, and the coloured stools suffice to distinguish even extreme instances of icterus neonatorum from cases of septic or catarrhal jaundice, and from those which depend on Buhl's disease, syphilitic disease of the liver or congenital obliteration of the bile-ducts.

The prognosis is invariably good; no treatment is necessary.

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REFERENCES

1. ASHBY. *Medical Chronicle*, 1885, vol. i. No 1.—2. BIRCH-HIRSCHFELD. *Gerhardt's Handb. der Kinderkrankheiten*, Bd. iv 2, 1879, S. 676, and *Virchow's Archiv*, 1882, Bd. lxxxvii. S. 1.—3. BOUCHUT. *Maladies des nouveau-nés*, 1885, p. 631.—4. COHNHEIM. *Lectures on General Pathology*, New Syd. Soc. Transl. vol. iii. p. 901.—5. CRUSE. *Arch. für Kinderheilkunde*, 1880, Bd. i. S. 353.—6. EPSTEIN *Volkmann's Sammlung klin. Vortrage*, 1880, No. 180.—7. FRERICHS. *Klinik der Leberkrankheiten*, 1858, Bd. i. S 199.—8. HALBERSTAM. *Beitrag zur Lehre vom Icterus Neonatorum*, Diss. Dorpat, 1885.—9. HOFMEIER. *Zeitschr. fur Geburtsh. und Gynaek.* 1882, Bd. viii S. 287 – 10. HOFMEISTER and BIRCH-HIRSCHFELD. *Virchow's Archiv*, 1882, Bd. lxxxvii. S 1.—11. L EMMETT HOLT. *Diseases of Infancy and Childhood*, 1897, p. 76.—12. KEHRER. *Oesterr. Jahrbuch fur Padiatrik*, 1871, Bd ii. S. 71.—13. PARROT and ROBIN. *Revue mensuelle de médecine et chirurgie*, 1879, No 5.—14. PORAK. *Ibid.* 1878, Nos 5, 6, and 8.—15. QUINCKE. *Arch. für exper Pathologie u Pharmakologie*, 1885, Bd. xix. S 31. 16 RUNGE. *Die Krankheiten der ersten Lebenstage*, 2 Aufl. 1893, S 216.—17. SILBERMANN. *Archiv für Kinderheilkunde*, 1887. Bd viii S. 101.—18 VIRCHOW *Gesammelte Abhandlungen*, 1856, S. 858.—19. WEBER. *Beitrage zur patholog Anat. d. Neugeborenen*, 1851, 3 Lief S 12

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DISEASES OF THE PANCREAS

THAT the pancreas not infrequently proves a source of serious and often fatal disease has become especially apparent within the past few years. The significance of hæmorrhage within this gland, or in its vicinity, was made prominent by Zenker in 1874, and his observations have been confirmed by those of Prince, Draper, and others. The concurrence of pancreatic disease and diabetes, at first recognised by Cowley, was made especially conspicuous by Lancereaux, and was demonstrated by the experiments of von Mering and Minkowsky. The attention given of late years to the physiology and pathology of this organ has shown that the so-called characteristic symptoms of disturbances of function of the gland, namely, fatty stools and lipuria, excessive salivation and watery dejections, bronzed skin, and cœliac neuralgia, and excessive emaciation, are in no way limited to diseases of the pancreas. Recent investigations lead to the conclusion that there are no pathognomonic symptoms of disease of this gland, although the presence of glycosuria should arouse the suspicion that the pancreas may be diseased. Attention should be called, however, to the statement by Walker, that disease of the pancreas, even when the liver is normal, may cause colourless stools. The affections which have been most thoroughly studied are pancreatic hæmorrhage and inflammation, calculi, cysts, and cancer. These I shall consider in the order in which I have enumerated them.

Pancreatic hæmorrhage.—The names pancreatic hæmorrhage and pancreatic apoplexy are applied to the occurrence of bleeding, usually within the pancreas, from rupture of its vessels: this bleeding not infrequently extends to the subperitoneal fat in the vicinity of the pancreas, and to the cavity of the lesser omentum.

Etiology.—Slight degrees of pancreatic hæmorrhage are occasionally found in cases of obstruction to the venous outflow, and in those diseases, infectious or not, in which minute hæmorrhages are wont to appear in various parts of the body. There is no satisfactory explanation, other than trauma, of the cause of serious pancreatic hæmorrhage. It occurs most frequently in persons beyond middle life, although it may be seen in young adults. It has been found rather more often in fat than in lean persons. Although more commonly present in persons addicted to the excessive use of alcoholic liquor, it has been observed also among the temperate or abstemious. There is nothing in age, sex, habits, condition, or previous disease of the individual which makes it possible to apprehend the probable occurrence of this lesion.

Morbid anatomy.—In the grave form of pancreatic hæmorrhage the source of the bleeding has not been discovered: no rupture of a large vessel has been found. The blood is infiltrated into larger or smaller portions of the gland, one or several centres being affected. The head alone may be the seat of the hæmorrhage, or the bleeding may be limited to the body or to the tail; the portion of the gland infiltrated with blood may be enlarged, dense, of a purple colour; or of normal size, soft, and friable. The presence of reddish yellow spots, and the recognition in them of crystals and granules of hæmatoidin, give suggestive evidence of a previous occurrence of the hæmorrhage. The gland-cells may show no abnormal appearances, or may be found granular or fatty. When the hæmorrhage occurs in fat persons the interstitial fibrous tissue of the pancreas is usually in a state of fatty infiltration. If the bleeding extend beyond the region of the pancreas it is frequently continued into the root of the mesentery, into the fat of the omentum, and into that behind the colon or around the kidney.

Symptoms.—In the non-traumatic cases unexpected abdominal pain is the most frequent incipient symptom. It is usually severe or intense, but may be slight or insignificant. Although sometimes referred to the epigastrium, it is often regarded as a colic, and is not sharply localised. In some cases a sense of constriction in the lower part of the chest is complained of. Neither nausea, vomiting, constipation, nor diarrhœa is of sufficient frequency to suggest a conspicuous lesion of the digestive apparatus. The symptoms which are suggestive of the nature of the lesion are those of collapse, characterised rather by feeble pulse and dyspnœa than by disturbance of intelligence; and they may lead immediately to death or persist for a period of some hours.

Prognosis.—That recovery from pancreatic hæmorrhage sometimes occurs is indicated by the evidence of antecedent hæmorrhage in the form of hæmatoidin granules and crystals and by the history of earlier mild attacks of symptoms like those above mentioned. The severer attacks are usually fatal, either within a few minutes or in the course of twenty-four hours. If the patient's life be prolonged beyond the latter period the case is no longer one of simple hæmorrhage, but becomes one of combined hæmorrhage and inflammation, which will be considered under the subject of acute pancreatitis. Even the severer varieties may not be absolutely hopeless, and patients attacked by pancreatic hæmorrhage, demonstrated by laparotomy, have recovered both from this operation and from the lesion.

Treatment.—The relief of pain and the stimulation of the patient are the especial indications for treatment. For the former the administration of morphia is required, usually subcutaneously, in quantity sufficient to control the pain. Alcoholic stimulants, the subcutaneous injection of $\frac{1}{60}$ of a grain of sulphate of strychnia, and the use of one-drop doses of a one per cent solution of nitro-glycerine are indicated in the treatment of the symptoms of collapse. No intentional attempt to treat the early stages of pancreatic hæmorrhage radically by surgical procedure has been made.

Pancreatitis.—It is noteworthy that the pancreas may be the seat of such parenchymatous changes as granular degeneration of the cells, multiplication of the nuclei, and redness and swelling of the gland. These conditions have been observed in the infectious diseases, but they are incapable of recognition by means of clinical manifestations. The occurrence of more extreme alterations—such as extensive implication of the interstitial tissue, frequent characteristic changes in the parts remote from the pancreas, and the association of symptoms which have led repeatedly to a recognition of the inflammation of the pancreas—demand a conspicuous place for pancreatitis in modern text-books on medicine. Acute and chronic varieties of this affection are to be considered. The former include the hæmorrhagic, gangrenous, and suppurative forms; the latter fibrous pancreatitis with its several complications, a state which is of especial significance in connection with its probable intimacy of relation to certain varieties of saccharine diabetes.

Acute pancreatitis.—There are two kinds of acute inflammation of the gland. The one represents a combination of inflammation and hæmorrhage, the more frequent termination of which is gangrene; the other is independent of hæmorrhage, and is characterised rather by suppuration than by gangrene.

Etiology.—Acute pancreatitis usually occurs in adult males, especially in those beyond middle life, and particularly in very fat persons. Although in many of the reported cases the free use of alcohol is noted, it is not probable that this agent acts otherwise than as a disposing cause. More important are antecedent and frequently recurrent attacks of gastro-duodenal catarrh, and injury from external violence. It seems probable that the catarrhal inflammation extends continuously from the duodenum along the course of the pancreatic duct.

Morbid anatomy.—The pancreas is enlarged either throughout its length or at one extremity, especially at the head. Its colour varies from a slight but uniform redness to a dark red, sometimes reddish black; the darker shades of red being found in the hæmorrhagic and gangrenous varieties of pancreatitis. The hæmorrhages are usually present in patches of various size, and are sometimes so considerable as to produce a swelling half the size of the fist. In such cases a section of the pancreas shows a variegated surface: patches of red, gray, and yellow can be seen. A further variety of colour often results from the presence of opaque white spots and lines due to a necrosis of the pancreatic fat-tissue. The pancreatic duct is usually patent throughout, but may contain a thick fluid more or less intimately mixed with blood. In the hæmorrhagic variety evidences of more or less extensive bleeding are to be found in the fat around the pancreas, especially near its head, and in the subperitoneal fat of the omentum, root of the mesentery, mesocolon, and in the region of the left kidney. Small patches of necrosis of the subperitoneal fat are common. If gangrene follow, more or less of the gland is transformed into a dark gray mass, which tends to become spongy and to form a slough, in some cases attached to the abdominal wall by a few shreds of tissue only. The peritoneal surface of the diaphragm, of the lesser omental cavity, and of neighbouring coils of intestine is covered with a fibrinous false membrane forming adhesions. The omental bursa (lesser sac of the peritoneum) frequently contains offensive blood-stained fluid, in which detached masses of necrotic fat may be found. Evacuation of the contents of this circumscribed peritoneal abscess may take place through a perforation into the stomach or duodenum. In suppurative pancreatitis the enlarged pancreas contains single or innumerable abscesses. The peritoneal covering of the pancreas is likely to become involved in the inflammation, which becomes extended to the peripancreatic tissue and to the walls of the lesser peritoneal pouch. Extensive suppuration may thus be produced, and evacuation of the pus by the stomach or duodenum occur. Fat-necrosis is rare in suppurative inflammation of the pancreas.

Thrombosis of the splenic vein is of frequent occurrence, the thrombus perhaps extending from the spleen to the portal vein, and sometimes being in a state of puriform softening. Variations in the size and consistency of the spleen are frequent, but enlargement, even when the splenic vein is obliterated, is inconstant Abscesses of the liver are more common in suppurative than in hæmorrhagic or gangrenous pancreatitis. Despite the frequent, almost constant, occurrence of a circumscribed peritonitis, extensive inflammation of the general peritoneum is rare. When the peritoneal surface of the diaphragm is affected, the inflammation may extend to the pleura and pericardium. On microscopical examination many of the lobules present the appearances characteristic of a coagulation-necrosis, and the interstitial tissue is extensively infiltrated with red blood corpuscles, leucocytes, fibrillated and granular material. Red blood corpuscles and leucocytes are also to be found in the ducts. Bacteria, especially the colon bacillus, first recognised in this affection by Welch, are found in the inflamed gland and in the focuses of fat-necrosis.

Owing to the important relation which multiple disseminated fat-necrosis bears to disease of the pancreas, it is desirable to call particular attention to this condition. Subperitoneal fat-necrosis, combined with evidences of hæmorrhage or inflammation, is almost invariably found in connection with pancreatitis, and with it alone. This relation is so constant as to indicate the importance of disease of the pancreas in its etiology, and to raise a doubt of the thoroughness of the examination of the pancreas in those cases where subperitoneal fat-necrosis is stated to have occurred in the absence of pancreatic disease. Langerhans has injected the minced pancreas of a rabbit into the subcutaneous fat of another rabbit with the production of fat-necrosis. Whitney, of the Harvard Medical School, succeeded in producing hæmorrhagic pancreatitis and fat-necrosis in a dog. Hildebrand produced typical fat-necrosis in the pancreas, the omentum, and the mesentery, by experiments on the pancreas of cats. *Such evidence corroborates the previously maintained* etiological importance of acute disease of the pancreas in the production of multiple, disseminated fat-necrosis.

Symptomatology.—Acute pancreatitis usually begins unexpectedly with severe symptoms. The patient, previously well, or at the most having suffered from some irregularity of digestion, is seized with abdominal pain, often severe, even intense, and either persistent or paroxysmal. The pain is usually in the epigastric region, and is sometimes referred to the region of the pancreas, although generally it is not sharply defined. In rare instances of suppurative pancreatitis the onset of the disease is gradual with little or no pain.

Vomiting closely follows the pain, and is occasional, constant, or repeated. It may be copious, and the vomit consists of partly digested food or of slimy matter. It may become green or black, and at times contains liquid or clotted blood. Slight or severe degrees of collapse usually follow the initial pain and vomiting. Chills occasionally occur at the outset, but more frequently take place later in the disease, especially in suppurative pancreatitis, in which variety they may be frequent and irregular.

The temperature is likely to become elevated in the course of twenty-four hours, and, as a rule, it ranges from 100° to 104° F. throughout the disease; but in rare cases there may be no definite rise. In suppurative pancreatitis exacerbations and remissions may take place, the course of the fever being irregular. Hiccough sometimes occurs, and mild degrees of delirium may appear. Slight jaundice also takes place occasionally, and the urine may contain albumin and casts. The upper part of the abdomen usually becomes swollen and tympanitic, and at times, as noted by Elliot, gives evidence of a deep-seated circumscribed resistance in the region of the head of the pancreas, where tenderness may be found on palpation. Deep pressure on the intercostal spaces in the region of the spleen may be painful. If the patient survive the initial symptoms, the subsequent course of this disease is that of a localised peritonitis. The abdominal swelling increases in size, even to an enormous degree, and is either general or limited to the epigastrium or to the left half of the abdomen. The distended abdomen is usually tympanitic, but it may be dull in the flanks. Moderate abdominal pain, at first apparent in painful and tender spots, and due to disseminated fat-necrosis, becomes more general. Vomiting and diarrhœa are frequent, and the patient loses flesh and strength. A severe paroxysm of lancinating pain may supervene during the third or fourth week, followed by frequent and copious discharges from the intestine, and disappearance of the abdominal swelling as the exudation from the bowels is evacuated. In the most prolonged cases of suppurative pancreatitis extending over a period of months, ascites or anasarca may occur; and a bronzing of the skin and glycosuria have been noted.

Diagnosis.—Acute pancreatitis is to be suspected when a previously healthy person or a sufferer from occasional attacks of indigestion is *suddenly seized with violent pain in the epigastrium followed by vomiting and collapse, and in the course of twenty-four hours by a circumscribed* epigastric swelling, tympanitic or resistant, with slight elevation of temperature. Circumscribed tenderness in the course of the pancreas and tender spots throughout the abdomen are valuable diagnostic signs. The action of an irritant poison is excluded by the history of the case and by an examination of the vomit. A perforating ulcer of the stomach or duodenum is eliminated by the absence of pain after eating and of hæmorrhages from the stomach or intestine. The seat of the pain and tenderness, and the absence of previous attacks of biliary colic and jaundice, are useful in excluding a diagnosis of gall-stones.

Acute pancreatitis in its early stages most frequently suggests acute intestinal obstruction; it is distinguished, however, by the severity of the onset, by the absence, in the early stages, of distension of the intestine, by the localised tenderness, if present, in the region of the pancreas, and by the infrequency of obstruction of the small intestine in the epigastrium. The patency of the large intestine may be determined by inflation or injection. In the later stages of acute pancreatitis, the physical characteristics due to the associated inflammation of the lesser sac of the peritoneum are suggestive of a cyst of the pancreas; but the severity of the earlier symptoms, the septicæmic characteristics of the later stages, the more acute course, and, when necessary, an exploratory puncture, suffice to set aside pancreatic cyst.

Prognosis.—Although acute pancreatitis has been shown to be a disease of extreme gravity, yet it must be admitted that mild cases occur. Similar but less severe symptoms have been recorded at an earlier date, in cases eventually proving fatal: when on autopsy hæmatoidin crystals and granules and fibrous thickening give evidence of previous hæmorrhage and inflammation. Osler and Korte have reported cases in which laparotomy established the diagnosis of acute pancreatitis in patients who recovered from both operation and disease. Trafoyer's patient was alive seventeen years after the sloughing pancreas had been discharged from the bowel. The circumscribed nature of the resultant peritonitis, and its successful treatment in rare instances by drainage of the abscess, make it probable that with greater accuracy of diagnosis, a more favourable prognosis may become possible. In rapidly fatal cases death from collapse results in a few days If the patient survive this period, death from septicæmia usually occurs in the course of one or two months. If the patient's life be prolonged for six months or a year, death may result from progressive emaciation and debility, or from diabetes.

Treatment.—The early stages of acute pancreatitis demand the subcutaneous injection of morphine to assuage the pain, and the use of stimulants by the mouth or rectum to relieve the symptoms of collapse. The preservation of the patient's strength by easily digested, nutritious food, by milk and broths, with the addition of farinaceous diet if possible, is essential for the eventual surgical treatment of this affection. The *latter course is indicated as early as the second or third week of the disease, if there is reason to believe that a peritonitic exudation, limited* to the boundaries of the lesser peritoneal cavity, exists. Thayer has reported a successful operation by Finney on the twelfth day.

Chronic pancreatitis.—Although suppurative inflammation of the pancreas not infrequently assumes a chronic course, extending over a period of many months, and may result in a considerable increase of fibrous tissue in the gland, its symptoms are distinctly those of a suppurative process. Induration of the pancreas may result from chronic obstruction to the portal circulation or from obstructive disease in the heart or lungs, but with symptoms quite subordinate to those occurring elsewhere. There is a genuine chronic fibrous pancreatitis, on the other hand, which pursues a latent course, is associated usually with disturbances of digestion, and of late years has received much attention on account of its frequent connection with saccharine diabetes.

Etiology.—The occasional presence of a fibrous thickening of the pancreas in infants is attributable to congenital syphilis, but it is not known that acquired syphilis may give rise to it. Although alcoholic excesses have been assumed to be among the causes of fibrous pancreatitis, the characteristic appearances of the latter affection are not often found in drunkards. The most probable cause is a chronic catarrh of the pancreatic duct, continued from the duodenum into the pancreas, which in certain cases may be due to the abuse of alcohol: this assumption is based rather upon the frequency of antecedent and persistent symptoms of chronic gastro-duodenal catarrh than upon the presence of morbid changes in the wall of the duct. Obstruction and dilatation of the duct result in fibrous atrophy of the gland. A fibrous thickening of parts of the pancreas is often associated with ulcer of the stomach or duodenum, tumours of the stomach or suprarenal capsule, aneurysm of the aorta or cœliac axis, or with disease of the spine.

Morbid anatomy.—The increase of fibrous tissue takes place throughout the gland or is limited to certain portions of it, especially to the head. The size of the pancreas may become so increased as to suggest a tumour, particularly a cancer of this organ. More frequently, in consequence of the contraction of the interstitial tissue, the pancreas is found diminished in size. The surface is smooth, nodular, or granular, and is of a reddish gray or grayish white colour. The consistency becomes increased; at times it is of the density of cartilage. The subperitoneal fibrous tissue in the neighbourhood of the pancreas, especially around the cœliac axis, at the root of the mesentery and near the suprarenal capsule, may be thickened and indurated. On section of the pancreas the surface is either more homogeneous or more finely granular than normal, according as the lobules are diffusely infiltrated with fibrous tissue or project in consequence of the contraction of the latter. A speckled yellow appearance is indicative of associated fatty degeneration of the gland-cells. Klebs has found within the fibrous tissue small white streaks or spots containing calcareous granules and crystals of fat-acids resembling those occurring in fat-necrosis.

The pancreatic duct may appear normal even when the pancreas is considerably enlarged; or it may be dilated, tortuous, and more or less sacculated; especially when inflammation or obstruction of the duct seems to be the cause of the pancreatitis. The presence of concretions and the formation of cysts deserve separate consideration.

Symptoms.—Digestive disturbances, epigastric pain and tenderness, and progressive loss of flesh and strength are the symptoms which occur in fibrous pancreatitis, and may precede death for months or years. The digestive disturbances consist of loss of appetite, nausea, vomiting (rarely), belching, pyrosis, and a sense of epigastric fulness and weight. These symptoms, usually attributed to gastric catarrh, in rare instances may be absent. Diarrhœa frequently exists; the dejections are sometimes fatty and may be colourless even when there is no jaundice. Jaundice occasionally occurs, and is persistent if the common bile-duct be compressed by the contracted head of the pancreas.

The epigastric pain is deep-seated, dull, burning or boring in character, perhaps paroxysmal; and if severe, is associated with extreme anxiety, restlessness, and a sensation of faintness. Epigastric tenderness has been observed, especially on the left side, and resistance either defined to the right of the median line or extending outward to the left. Enlargement of the spleen sometimes occurs, and a moderate degree of ascites. A most important symptom, if present, is glycosuria, for the disease then is likely to put on the character of a severe diabetes.

Cowley, in 1788, first reported a case of diabetes associated with pancreatic disease (calculous), and Lancereaux in 1877 maintained that there is a pancreatic diabetes characterised by polyuria, polyphagia, polydypsia, rapid loss of flesh and strength, and dependent upon grave alterations of the pancreas; von Mering and Minkowsky in 1890 demonstrated that complete extirpation of the pancreas in dogs immediately produced a severe form of rapidly fatal diabetes. Their observations were almost simultaneously confirmed by de Dominicis, and since then by numerous experimenters, and upon various animals. According to Minkowsky, when a relatively small amount of pancreas remained in the body, the diabetes was only moderately severe; if one-eighteenth to one-twelfth of the gland were left, a sort of alimentary glycosuria alone resulted; if more than one-tenth of the gland was left, there was ordinarily no glycosuria. Minkowsky maintains that the diabetes results from the loss of a "glycolytic ferment," a sugar-destroying agent produced in the pancreas and absorbed by the lymphatics of this gland. It is claimed by de Dominicis, on the contrary, that this variety of experimental diabetes is the result of disturbed tissue-metamorphosis caused by the absence from the intestine of pancreatic juice, a view based in part upon the production of glycosuria by simple ligature of the duct of Wirsung. Williamson has collected one hundred cases of diabetes in which pancreatic lesions were noted: in thirty-nine there was more or less atrophy; in eight the atrophy was very marked; in thirteen there was extensive fibrous thickening, while fatty degeneration with or without fibrous thickening and calculi, cysts with or without calcification and fibrous thickening, hæmorrhagic and suppurative pancreatitis, made up the balance. Hansemann, although recognising that the pancreas may be diseased either from acute inflammation, sclerosis, lipomatosis, calculi, or cancer, explains the absence of diabetes in these cases by the probable presence of a sufficient number of functionally active cells to permit the physiological action of this gland upon the glycolytic process. Hence, although various alterations of the pancreas, especially fibrous atrophy, have been found associated with diabetes, it is to be remembered that extensive lesions of the pancreas may exist without diabetes, and that the latter disease often occurs without disease of the pancreas.

Prognosis.—The prognosis of chronic fibrous pancreatitis is necessarily grave since we have no evidence that reproduction of this gland is possible. It is to be recognised, however, that patients may live for years apparently in good health after the removal of a considerable part of the pancreas by operation, sequestration and evacuation; or after its atrophy from cystic degeneration or fatty infiltration. Of great value, as suggesting a favourable prognosis, are the experiments above mentioned, which show that a small portion of the pancreas suffices for the preservation of the health of many animals.

Treatment.—The treatment of chronic pancreatitis necessarily consists in the attempt to relieve the digestive disturbances by means of a diet which shall be least irritating to the duodenum, and which demands the least possible quantity of pancreatic juice for its digestion. As the pancreatic juice promotes the digestion of fat, a diet relatively free from fat is indicated. The use of raw minced pancreas and of pancreatin is to be recommended, since Abelmann has shown that after extirpation of the pancreas the digestion of fat is promoted by their use. When a chronic pancreatitis is suspected to be the cause of diabetes the diet should be largely nitrogenous and relatively free from farinaceous and saccharine articles of food. The frequent use of minced pancreas is indicated in such cases also, especially since experiments show that the retention of small portions of the gland, or the transplantation of a portion of the pancreas when the gland has been removed, may prevent glycosuria. According to Becher, carbonated waters increase both the flow and the proteolytic action of the pancreatic juice of dogs. The pancreatic secretion of rabbits was found by Gottlieb to be increased by the administration of dilute acids, oil of mustard, and spices.

Pancreatic calculi.—*Etiology.*—The mode of origin of stones in the pancreatic duct is presumably the same as in the case of gall-stones. A catarrhal condition of the pancreatic duct and retention of secretion are probably the chief factors in the precipitation of their constituents. The retention of secretion may be the result of a pathological process outside the duct producing obstruction to the escape of its contents; or, on the other hand, the duct may become obstructed and dilated by the stone.

Morbid anatomy. — The calculi chiefly contain carbonate of lime with some phosphate of lime, and, at times, cholesterin; they vary in size from grains of sand to that of a walnut. Not infrequently a mortar-like material is present. Single stones may be found impacted in the duct, or more than a hundred may be present. Their shape is usually rounded or oblong, sometimes elongated and branching. They are of a light gray or white colour, and their surface smooth, rough, or spinous. The concretions, though tough, are usually easily crushed into irregular fragments.

Not only are the duct of Wirsung and its branches commonly dilated, but atrophy and induration of the pancreas, and sometimes fistulous communications with the stomach, duodenum, or peritoneal cavity, are, at times, associated with stone. Cancer of the pancreas is present also in rare cases.

Symptoms.—Calculi may exist in the pancreas without any definite evidence of their presence. As a rule, symptoms of gastric or gastro-duodenal indigestion precede those due to the presence of the stone. These latter are attacks of pain associated with the incarceration or escape of the stones, or a complex group of symptoms dependent upon the secondary changes occurring in the pancreas. The pain is either dull, giving a sense of pressure sharply defined to a limited spot of the epigastrium, or it may be intense and paroxysmal, radiating along the left costal border toward the spine and the left shoulder-blade. The seat of the pain is not especially sensitive. The paroxysms resemble those produced by gall-stones, and are sometimes accompanied by jaundice. Indeed, gall-stones and pancreatic stones may coexist in the same person. Minnich notes that his patient, who previously had suffered from very severe attacks of biliary colic due to typical pigmented gall-stones found in the stools, could not discriminate these attacks of colic from those in which concretions apparently pancreatic were discharged. Although it may not be possible to distinguish between some attacks of pancreatic and of biliary colic, the symptoms which result from the prolonged presence of pancreatic calculi are wholly different. They resemble those mentioned as a result of fibrous pancreatitis, which condition often accompanies pancreatic calculi. The patient loses flesh and strength . the dejections are often liquid, contain abundant fat-acids, an excess of undigested muscular fibre, and sometimes concretions which present the characteristics of pancreatic stones. More significant is glycosuria, either intermittent or persistent. Rarely a cystic tumour may develop in the epigastrium after the local pain has disappeared.

Diagnosis.—The presence of pancreatic calculi is to be inferred from severe attacks of deep-seated epigastric pain radiating to the left, simulating biliary colic, but without jaundice; followed by the evacuation of concretions resembling those above described, and, in the course of years, by progressive loss of flesh and strength and by glycosuria. Minnich confirmed his diagnosis by the discovery of the concretions in the stools; and an autopsy established the diagnosis of Lichtheim which was based provisionally on the occurrence of diabetes after the attacks of colic.

Prognosis.—Recovery may follow the evacuation of pancreatic calculi through fistulous communications with the stomach or duodenum, or, as seems probable in the case reported by Capparelli, with the abdominal wall. More commonly the prognosis is that of chronic pancreatitis with frequent resultant diabetes, or of pancreatic cyst. An immediately fatal result following peritonitis from perforation is a rare incident.

Treatment.—The attack of pancreatic colic is to be relieved by morphine, ether, or chloroform, and the external application of heat as in the case of biliary colic. Holzmann states that the attacks of colic disappear after the injection, three times a week, of 1 c.c. of a 1 per cent solution of pilocarpine. The medical treatment of the remoter effects of the stones is that mentioned for chronic pancreatitis. With the possibility of forming an early diagnosis will come the opportunity for the surgeon to remove the concretions before the incurable results of their presence take place.

Cysts of the pancreas.—Under this term have been included a variety of lesions which in the main have been regarded as due to dilatation of the duct of Wirsung. It is probable, however, that many reported cysts of the pancreas were circumscribed collections of fluid wholly outside the pancreas, and that other varieties of cysts of the pancreas occur besides those due to dilatation of its duct.

Etiology.—As a rule, pancreatic cysts in the adult occur with equal frequency in the two sexes. Richardson's case of the extirpation of a cyst presumably pancreatic from a child of fourteen months is unique, and suggests that, at times, these tumours may be of congenital origin. Pye-Smith also reports a case suggestive of a similar etiology. The conspicuous place given to traumatism in the etiology of pancreatic cysts is, as advocated by Lloyd, probably due to a confusion of peritonitis limited to the lesser peritoneal cavity with cysts of the pancreas. It is possible that injury may produce an acute pancreatitis, resulting in an obstruction to the duct with subsequent dilatation; it seems more probable that the resultant acute pancreatitis becomes extended to the peritoneal covering of the pancreas, which forms the posterior wall of the smaller sac of the peritoneum. More important in the etiology of the genuine pancreatic cyst is the extension of inflammation from the duodenum into the pancreatic duct, resulting in its obstruction. The most common variety is that due to obstruction and dilatation of the duct with retention of its contents. The obstruction may result from inflammation within or without the wall of the duct, from the pressure of tumours or the presence of calculi. Durante's case of assumed pancreatic cyst from obstruction of the duct of Wirsung by a lumbricus is unique. It is possible that the lesion in this patient may have been an inflammation of the lesser peritoneal pouch secondary to a pancreatitis. Rarest of all is the neoplastic cystoma of the pancreas.

Morbid anatomy.—A cyst may arise in any part of the pancreas;

there may be one or many cysts, varying in size from those almost microscopic to others as large as a pregnant uterus at full term. When large, a spherical tumour is formed which does not suggest the pancreas; or numerous small cysts may be grouped along the course of this gland. *They lie behind the lesser peritoneal cavity*, the walls of which at times are fused with them. The inner surface of the cyst-wall is smooth or trabeculated, often contains openings communicating with smaller cysts, sometimes bears papillary outgrowths, and is lined with cylindrical epithelium. At times the duct of Wirsung is to be followed from the duodenum, and from the tail of the pancreas to the interior of the cyst; or again the duct may be obliterated. The largest cysts may contain fourteen quarts of fluid: this is of a grayish colour, slightly opaque, viscid or watery, alkaline, of a specific gravity from 1010 to 1024. On microscopical examination, leucocytes, epithelial cells in a state of fatty degeneration, fat-drops, cholesterin and acicular crystals may be found. The fluid may emulsify fat, saccharify starch, and digest albumin and fibrin like pancreatic juice; the older the cysts, the less likely are all these reactions to be present. Much diagnostic importance often is attached to these characteristics; but Boas asserts that other fluids possess diastasic and emulsifying qualities, while even in the fluid contents of a pancreatic cyst the peptonising power may be absent or slight. The presence of blood in the cysts has likewise been regarded as of marked diagnostic importance. This view is based particularly upon the appearance of the fluid from assumed cysts of the pancreas of traumatic origin. As has already been stated, such accumulations of fluid, even if they present the properties of the pancreatic juice, may be due to an encysted peritonitis of the peritoneal covering of the pancreas the ducts of which may be opened. Typical pancreatic cysts may contain no blood, and circumscribed collections of bloody fluid in the vicinity of the pancreas may lie wholly outside this gland. Although multiple cysts of the pancreas are usually retention-cysts, the cases reported by Salzer and Hartmann suggest that the pancreas, like the ovary, may give rise to cystoma. That cystoma of the pancreas may be malignant as well as benignant is indicated by the case reported by Hartmann and Gilbert.

As the pancreatic cyst increases in size it causes atrophy of the gland, the lobules of which are to be found in its wall; or it may project from the pancreas as a pedunculated tumour. The stomach is usually pushed upwards, more rarely downwards, and the transverse colon lies in front or below. A small cyst may lie to the left or right of the median line according to the part of the pancreas from which it arises. The larger cysts usually occupy first the epigastric and the left hypochondriac regions; but they may extend into the right hypochondrium, and the lower border may be found at the brim of the pelvis. The anterior wall of the cyst may be fused with the posterior wall of the stomach, rendering extirpation difficult, if not impossible. Rupture of the cyst may take place into the lesser peritoneal sac, into the general peritoneal cavity, or into the stomach. Rupture into the lesser cavity may explain the presence of a large cystic tumour, communicating with the interior of the pancreas in those cases in which a considerable portion of the organ remains unaltered.

Congenital cystic disease of the pancreas may be associated with cystic disease of the liver and kidneys.

Symptoms.—There may be no symptoms suggestive of a cyst of the pancreas before the recognition of an abdominal tumour. With its appearance, however, symptoms of a more or less serious character usually occur. These may be unimportant until the cyst has attained a large size, for the tumour has been accidentally discovered, in persons apparently healthy, after child-birth or during convalescence from typhoid fever.

As a rule, however, the patient suffers from attacks of epigastric pain, perhaps constant and severe, with symptoms of collapse. The pain may last for hours, days, or weeks, and may extend perhaps over a period of years. It may radiate from near the ensiform cartilage either downwards or laterally, especially toward the left side; or may extend into the left shoulder or into the left half of the face. The painful paroxysms may have no apparent cause, or may follow an error in diet, when belching, vomiting, diarrhœa, or constipation occurs, and the patient complains of a sensation of fulness in the epigastrium which may be tender to the touch. The attacks of pain may be followed by jaundice, and recurrent intestinal hæmorrhage has been observed. Strength and nutrition are unaffected, or weakness and emaciation may appear.

Although the cyst usually is of slow growth and may remain quiescent for years, even becoming smaller for a while, it may appear soon after an attack of pain and vomiting, and rapidly enlarge within a few months. When hæmorrhage takes place from its wall the cyst may attain the size of a child's head within a fortnight. Commonly it is observed first in the left hypochondrium between the costal cartilages and the median line; and, as it enlarges, it causes a swelling of the upper half of the abdomen which may extend from the ensiform cartilage to the pubic symphysis and into each flank, and is of globular shape, resistant, inelastic, and smooth on the surface. As a rule the cyst is slightly movable both vertically and laterally, and often transmits the beat of the aorta, but has no expansile pulsation. It is dull on percussion where not overlain by stomach or intestine, and on auscultation a systolic souffle transmitted from the adjacent aorta is sometimes heard. The smaller and more deeply-seated the cyst, the more likely is it to suggest a solid tumour; although, when large and superficial, fluctuation may be present. The pressure of the contained fluid may be such that the liquid will spurt several feet from a trocar plunged through the wall.

As the tumour becomes apparent the epigastric pain and digestive disturbances are likely to be more persistent, and the larger its size the greater the loss of flesh and strength. The cyst may be so large or so situated as to interfere with the descent of the diaphragm and to produce dyspnœa; or it may press upon the portal vein or inferior vena cava and cause ascites or anasarca. By compression of the intestine it has produced symptoms of obstruction of the bowels. In rare instances fat and an excess of undigested muscular fibre have been found in the fæces, and albumin or sugar in the urine.

Diagnosis.—Physical are more important than rational signs in establishing the diagnosis of cyst of the pancreas. A smooth, rounded tumour is to be recognised, first appearing in the epigastrium or left hypochondrium, slightly movable especially vertically, and usually separated from the liver and spleen by a resonant area. Inflation of the stomach shows that the tumour lies behind and usually below this organ. Inflation of the colon gives evidence that the latter either crosses or lies below the tumour. Exploratory puncture permits the escape, under high pressure, of an alkaline fluid which may be more or less bloody, and which usually emulsifies fat, transforms starch into glucose, and may digest albumin and fibrin. The continued escape of such a fluid after the establishment of drainage is in favour of the pancreatic origin of the cyst. In the differential diagnosis solid tumours are easily excluded by exploratory puncture. The transmitted, non-expansile pulsation, disappearing when the patient is on the hands and knees, sets aside aneurysm of the aorta. A dropsical gall-bladder is continuous with the liver and lies in the right half of the abdomen. Hydronephrosis of the left kidney is manifested by an oblong tumour more limited to the left half of the abdomen than is a cyst of the pancreas, the lower border of which lies near the brim of the pelvis; and the inflated descending colon rather follows its length than crosses it transversely. Enormous cysts of the pancreas may be confounded with cystic ovarian tumours. The latter produce an increase in the size of the abdomen from below upwards, and the lowermost portion of the tumour is not overlain by the intestine. The aspirated contents are usually free from blood, are likely to be more gelatinous, and do not produce the above-mentioned reactions with fat, starch, and albumin.

It may be impossible to discriminate between collections of fluid in the lesser peritoneal sac (omental bursa) or in the mesentery and cysts of the pancreas. The former may arise from the pancreas, as the echinococcus cyst; or may be due to dilated lymphatics, as the chylous cyst; or, more frequently, may result from an inflammation caused by traumatism, perforating ulcer of the stomach or duodenum, or acute pancreatitis. It may not be possible to exclude serous or sero-hæmorrhagic inflammation of the lesser peritoneal cavity; but the character of the fluid may permit us to exclude suppurative peritonitis, an echinococcus cyst and a chylangioma.

Prognosis.—Cysts of the pancreas have persisted for twenty years, giving rise to but little disturbance. Even the larger cysts may interfere but slightly with the digestive process, although it is possible that diabetes may be the result. The larger cysts are especially dangerous from their liability to rupture, and to interfere mechanically with respiration, with circulation, and with the passage of food through the stomach and intestines.

Treatment.—The smaller pancreatic cysts accidentally discovered and producing no disturbance require no treatment. The larger cysts demand surgical treatment, either drainage or removal; the latter operation is preferable, but not always possible. Either operation usually results favourably, although the fistula consequent on the establishment of drainage often remains open for months.

Cancer of the pancreas.—Although tubercle, gumma, lymphoma and sarcoma may be found as tumours of the pancreas, they are of such rarity as not to require particular consideration; especially as the symptoms of lymphoma and sarcoma are virtually those of cancer.

Willigk and Lebert state that cancer of the pancreas occurs in about 6 per cent of all cancers. Dr. Herringham has made a study of 57 cases, and Mirallié has been able to collect 113 cases of primary cancer of the pancreas. According to the last observer and Segré, rather more than two-thirds of the patients are males. The affection occurs most frequently between the ages of thirty and fifty years, although it may be present in children and infants, and has been found at birth. Unlike cancer of the gall-bladder, it is rarely associated with calculi.

Morbid anatomy.—Any part of the pancreas may be the seat of cancer, although the head is usually affected; while other portions of the pancreas may show no abnormal appearances. It may form a circumscribed tumour the size of a child's head, or the entire gland may be infiltrated with the new growth. The colour varies in accordance with the greater or less abundance of fibrous tissue and epithelioid cells, the kind and degree of degeneration affecting the latter, the quantity of blood, the occurrence of recent and old hæmorrhages, and the presence of bile pigment. The consistency varies from that of soft encephaloid to the cartilage-like density of scirrhus. Dilatation of the duct of Wirsung may result from its peripheral obstruction or obliteration by cancer of the head of the pancreas, and obstruction of the common bile-duct also is frequently thus produced.

The disease is likely to extend to the adjacent lymphatic glands, and secondary nodules may be found in the liver or spleen. Invasion of the peritoneum also may occur, and adhesions are often found between the pancreas and the stomach, colon, small intestine, spleen, liver, and gall-bladder.

Symptoms.—There may be no suggestive symptoms, and cancer of the pancreas is sometimes found unexpectedly after death from other causes. The more characteristic symptoms may be preceded for years by disturbances of digestion, such as loss of appetite, belching, nausea, vomiting, and a sensation of epigastric fulness. In rare instances symptoms of pancreatic diabetes—polyphagia, polydypsia, glycosuria and emaciation —may be present. Paroxysms of pain also may occur, extending from the epigastrium into the back, and are often regarded as attacks of lumbago. According to Mirallié's analysis, jaundice and pain are the disturbances which most often immediately precede the graver symptoms of cancer of the pancreas. The jaundice, the result of pressure upon the common bile-duct, may appear suddenly or gradually; it usually persists and progressively increases in severity. It may be preceded by rigors and be accompanied by pain resembling biliary colic. The liver is frequently enlarged, and, when jaundice is present, the gall-bladder is usually dilated. Epigastric pain may precede or accompany jaundice, and is often transitory, but is intense in at least one-half of the cases. It may become continuous, or perhaps be interrupted by paroxysms; it comes without apparent cause, and is more frequent at night. It radiates as a cœliac neuralgia, and may be accompanied with a sensation of faintness and anxiety. The most characteristic sign is the tumour which, in from one-fourth to one-half of the cases, is to be observed in the epigastric or umbilical region, as a deep-seated, rounded or elongated, sometimes nodulated swelling, varying in density and defined with difficulty. It may be sensitive to the touch, and its mobility is slight. It is likely to transmit the aortic pulsation, and perhaps to cause a murmur, but it is not expansile. The cancer may produce obstruction to the flow of blood through the portal vein and cause ascites, or may press upon the inferior vena cava and cause dropsy of the lower extremities. In the former case the tumour may first become apparent after removal of the ascitic fluid. When obstruction of the duodenum is produced, dilatation of the stomach or intestinal obstruction may result. Hydronephrosis, from compression of the left ureter by cancer of the tail of the pancreas, is very rare. With the appearance of jaundice, cœliac neuralgia, and tumour, the disease rapidly advances. The appetite may remain unaffected, or may become even excessive. When vomiting is present the evacuated contents of the stomach may contain blood, free fat, or fat-acids. Constipation may be present, or the action of the bowels may be increased or irregular. The stools may contain, though rarely, liquid or solid fat or fat-acids; and blood may be present. More important, perhaps, is the presence of abundant undigested muscular fibre in the absence of diarrhœa. There may be polyuria, and the urine frequently contains albumin, more rarely sugar; although both glucose and maltose have been found, and glycosuria, after persisting for some time, may disappear shortly before death. When pancreatic juice does not enter the bowel, indican is diminished and ingested salol is not decomposed; but the evidence based upon these reactions is as yet somewhat contradictory and insufficient to make them of diagnostic importance. Although the general nutrition may remain but little affected till death occurs, emaciation and debility may be present and rapidly increase toward the fatal termination. The duration of the disease after its recognition is usually a matter of weeks or months, but it may continue a year or more. Death sometimes occurs suddenly from gastro-intestinal or intra-peritoneal hæmorrhage, or from pulmonary embolism.

Diagnosis.—The most important evidence is furnished by the tumour, and by the symptoms resulting from obstruction of the pancreatic duct and common bile-duct. The seat of the tumour is determined by inflation of the stomach and colon. It may be mistaken for cancer of the pylorus, duodenum, transverse colon, or liver. Cancer of the pylorus is more freely movable, and is more regularly associated with a dilated stomach: moreover, jaundice is less likely to occur. Cancer of the duodenum may produce the same symptoms as cancer of the pancreas, and, indeed, is in most instances due to an extension from the latter. Cancer of the transverse colon is more freely movable, and its seat is determined by inflation, while its symptoms are those of chronic intestinal obstruction. The presence of abundant indican in the urine is suggestive rather of intestinal cancer than of cancer of the pancreas. Cancer of the liver is more freely movable, more frequently associated with ascites, and more likely to be accompanied with enlargement of the organ; yet, as cancer of the pancreas lies nearly always in the head of it, jaundice is a frequent symptom of cancer in either viscus. The most satisfactory evidence, at present, of deficient pancreatic juice in the bowel is afforded by the abundance of undigested muscular fibre in constipated stools after a meat diet, and by the absence of carbolic acid in the urine when a drachm of salol is taken in divided doses during the day. Neither fatty fæces, lipuria, nor glycosuria is of especial value in the diagnosis of cancer of the pancreas.

Prognosis.—Always fatal. Death, as a rule, rapidly follows the occurrence of jaundice and ascites. It may occur within four weeks after the former, and within six weeks after the latter.

Treatment.—Symptoms are to be treated as they arise; the use of pig's pancreas has produced a diminution of the pain and of the jaundice.

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REFERENCES

1. Boas. *Berl. klin. Wochenschr.* 1891, xxviii. p. 40.—2. Capparelli. *Jahresber.* Virchow-Hirsch, 1883, p. 267.—3. Cowley. *London Med. Jour.* 1788, ix. p. 286.—4. Dominicis, de. *Gior. internaz. d. sc. med. Napoli*, 1889, N.S. xi. p. 801.—5. Draper. *Tr. Ass. Am. Physicians*, 1886, i. p. 243.—6. Durante. *Allg. med. Centr.-Ztg.* Berl. (*Abs.*) 1894, lxiii. p. 427.—7. Elliot. *Boston Med. and Surg. Jour.* 1895, cxxxii. p. 351.—8. Fitz. *Boston Med. and Surg. Jour.* 1889, cxx. p. 181.—9. Gottlieb. *Verhandl. d. naturh. med. Ver. zu Heidelb.* 1894, N.F.V. 203.—10. Hansemann. *Ztschr. f. klin. Med.* Berl. 1894, xxvi. p. 314.—11. Hartmann and Gilbert. *Congr. franc. de chir. Proc.-verb.* 1891, 618.—12. Herringham. *St. Barth. Hosp. Rep.* Lond. 1894, xxx. p. 5.—13. Hildebrand. *Centralbl. f. Chir.* Leipz. 1895, xxii. p. 1.—14. Holzmann. *Munchen. med. Wochenschr.* 1894, xli. p. 390.—15. Klebs. *Handb. d. path. Anat.* 1876, i. 2, p. 553.—16. Körte. *Arch. f. klin. Chir.* Berl. 1891, xlviii. p. 721.—17. Lancereaux. *Bull. Acad. de med.* Paris, 1891, 3 s. xxvi. p. 367.—18. Langerhans. *Festschr.* Rudolf Virchow, Berl. 1891.—19. Lichtheim. *Berl. klin. Wochenschr.* 1894, xxxi. p. 185.—20. Lloyd. *Brit. Med. Jour.* Lond. 1892, ii. p. 1051.—21. Mering and Minkowski. *Arch. f. exper. Path. u. Pharmakol.* Leipz. 1889-90, xxvi. p. 371.—22. Minkowski. *Arch. f. exper. Path. u. Pharmakol.* 1892-93, xxxi. p. 85.—23. Minnich. *Berlin. klin. Wochen.* 1894, xxxi. p. 187.—24. Miralliè. *Gaz. des hôp.* Paris, 1893, lxvi. p. 889.—25. Osler. *Principles and Practice of Medicine*, 1892, p. 459.—26. Prince. *Boston Med. and Surg. Jour.* 1882, cvii. p. 28.—27. Pye-Smith. *Tr. Path. Soc.* Lond. 1885, xxxvi. p. 17.—28. Richardson. *Tr. Am. Surg. Ass.* Phila. 1892, x. p. 211.—29. Salzer. *Ztschr. f. Heilk.* 1886, vii. p. 19.—30. Segré. *Centralbl. f. klin. Med.* 1888, xlviii. p. 884.—31. Thayer. *Am. Jour. Med. Sci.* 1895, cx. p. 396.—32. Trafoyer. *Wien. med. Wochenschr.* 1880, xxx. p. 139.—33. Walker. *Med. and Chir. Soc. Trans.* 1889, lxii. p. 25.—34. Welch. *Med. News*, Phila. 1891, lix. p. 669.—35. Williamson. *Med. Chron.* Manchester, 1891-92, xv. p. 367.—36. Zenker. *Deutsche Ztschr. f. prakt. Med.* Leipz. 1874, i. p. 351.

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DISEASES OF THE LIVER

ANATOMY OF THE LIVER

Topographical Anatomy.—The liver is the largest gland in the body, and the largest of all the abdominal organs. It occupies the right hypochondrium and the epigastric region, and frequently extends also int the left hypochondrium.

Its anatomical relations are both numerous and important.

Above it is in relation to the diaphragm, filling up its vault, and, through the diaphragm, to the lungs and heart.

Below it is in immediate relation to the stomach, the first part of the duodenum, and the transverse colon with its hepatic flexure; and, more posteriorly, to the suprarenal capsule and the head of the right kidney. The narrow edge of the left lobe overlaps and hides the lesser curvature of the stomach with its pyloric and cardiac orifices; a relation maintained irrespective of the degree of distension of stomach.

In front the greater part of it is covered by the diaphragm and the lower margin of the right lung protected by the costal cartilages and lower ribs (5th to the 9th); and it only comes into immediate relation with the abdominal walls over a small area occupying the subcostal angle.

Laterally on the right side it is protected by the lower ribs (7th to 11th inclusive); on the left it tails off over the stomach, and may extend into the left hypochondrium and come into relation with the spleen.

Its upper border is much curved, rising from the lower end of the sternum (base of the xiphoid cartilage) in the middle line to the upper border of the 5th rib in the mammary line, and then falling to the upper border of the 7th rib in the mid axillary line, of the 9th rib in the scapular line, and of the 11th rib in the dorsal line.

Its lower border corresponds on the right side in the mammary line with the lower edge of the costal arch, and stretches obliquely across the epigastrium in the region of the pit of the stomach at a somewhat varying level (7th to 8th costal cartilages), about midway between the umbilicus and xiphoid notch.

Relations on percussion.—The liver being for the most part in contact with organs containing air,—the lungs above and the stomach and colon below,—its boundaries can be more easily determined by percussion than is the case with any other organ in the abdomen. The only solid organ besides the kidney with which it is in close relation

— separated, however, by the diaphragm — is the heart with its pericardium. In the middle line up to the left, therefore, its upper limits cannot be determined by percussion. On the right side, where it is in relation to the right lung, they are easily determined. The *upper line of liver dulness* is curved, being found in the mammary line at the upper border of the 5th rib; in the mid axillary line two interspaces lower—namely, at the upper border of the 7th rib, in the scapular line at the 9th rib, and behind at the 11th rib. The dulness at these points is, however, not absolute, the lower edge of the lungs, especially in front, intervening between the liver and the chest wall for a varying distance, according to the degree of expansion of the lung. During quiet breathing the upper limit of absolute dulness in the mammary line is found about an interspace lower; namely, the upper border of the 6th rib. By forced inspiration the lung can be made to descend an interspace; namely, to the upper border of the 7th rib.

The *lower edge of the liver* is in relation throughout to air-containing organs, but its exact delimitation by percussion is rendered somewhat difficult by the circumstance that the relations obtaining at the upper border are here reversed. At the upper border the visceral mass is constituted by the solid liver, which is only slightly overlapped by a thin margin of resonant lung substance. At the lower border the visceral mass —stomach and transverse colon—is resonant, while the edge of the liver is for the most part thin and overlapping. This applies especially to that portion of the right and left lobes which comes into immediate contact with the abdominal wall. It overlies the stomach, and the dulness due to it is liable to be modified by the resonant note of the stomach subjacent to it.

In expiration and quiet breathing the lower limit of the hepatic dulness in the middle line is found about an inch below the xiphoid cartilage; the hepatic dulness at this point occupying the upper third of a line between the xiphoid cartilage and the navel. During deep breathing it descends an inch or an inch and a half, or even more; so that the dulness occupies approximately the upper two-thirds of the same line.

On the right side the lower limit of dulness is found, during quiet breathing, in the mammary line about the edge of the costal arch, half an inch above or below. From this it extends to the left somewhat obliquely upwards across the subcostal angle, from about the 9th costal cartilage on the right side to the 7th costal cartilage on the left. In the right axillary line it corresponds to the 10th intercostal space; in the right scapular line to the 12th rib, where, however, it becomes difficult to distinguish it from the dulness of the kidney.

Within the above limits the position of the liver is not fixed, but is much influenced on the one hand by the respiratory movements of the diaphragm, and on the other by the degree of distension of the other abdominal organs.

The foregoing boundaries and limits apply to the liver during expiration or quiet breathing.

During deep inspiration the liver is lowered an appreciable distance—according to Sibson as much as two inches, according to Murchison only half an inch. On the right side its lower edge descends an inch or more below the edge of the costal margin, while its left lobe descends as low as the upper two-thirds of the line between the navel and the tip of the xiphoid cartilage. As pointed out by Sibson, this greater prominence of the liver during inspiration is due not solely to the descent of the diaphragm, which pushes the liver downwards and slightly forwards, but also in part to the elevation and rotation outwards of the lower ribs and costal cartilages. In relation to the ribs the descent of the liver is thus greater than its actual descent in the abdomen. It is probable, also, that the lowering of the liver during forced inspiratory movements would be still greater but for the fact that the liver itself is compressible, and becomes somewhat flattened out from side to side by the force of the diaphragm, its blood being forced freely out of its hepatic veins into the right auricle.

The dulness over the right lobe is even more affected by forced inspiratory movements than over the left, being thrust downwards by the contraction of the right half of the diaphragm a distance of two inches or more below the costal margin.

The above delimitations apply to the adult healthy liver. It remains to be noted that in the new-born child, and in early infancy, the liver is relatively much larger than in the adult. At birth it occupies nearly one-half of the abdominal cavity. Below, the right lobe extends nearly to the iliac crest. Moreover, the left lobe is relatively much larger than in the adult, and extends across into the left hypochondrium, coming into contact with the abdominal wall and the spleen.

Nerve-supply.—The liver receives its nervous supply from the left pneumogastric nerve and the solar plexus of the sympathetic, both sets of branches entering through the portal fissure. Its nervous supply is thus the same as that of the stomach and intestines. The sympathetic branches accompany the hepatic artery; some also accompany the portal vein. Within the liver the nerves are distributed to the walls of the blood-vessels and biliary ducts, and pass also between the hepatic cells of the lobule, following the course of the bile canaliculi; they probably end in a fine network which ramifies between and over the liver-cells, as has been shown by Korolkow to be the case in animals.

The Bile-ducts take origin in minute canaliculi — intercellular passages—lying between and around the individual cells. A liver-cell is always interposed between canaliculus and capillary vessel. These canaliculi appear to be without any definite walls, and to have rather the character of intercellular channels. If they have walls, these are not distinguishable from the walls of the liver-cells between which they run. They form a network around the individual liver-cell, which is much finer and closer than that of the capillary network.

The most recent observations (Pflüger and Kupfer) seem to demonstrate even a closer relationship between the liver-cells and the canaliculi, for they show the existence of vacuoles within the liver-cell communicating by minute channels with the adjacent canaliculi.

Blood-supply.—The blood-supply of the liver is of a peculiarly rich character, being a double one; it flows partly through the portal vein, partly through the hepatic artery. Both these vessels enter the liver through its transverse fissure, and along with the biliary ducts their branches occupy the portal canals throughout the liver.

The branches of the portal vein ramify between the lobules (interlobular) and end in a capillary network within the lobule itself. Within the portal canals the branches of the portal vein receive small veins returning the blood distributed by the hepatic artery.

The hepatic artery is distributed (*a*) to the walls of the ducts and vessels and the surrounding connective tissue of the portal canals; (*b*) to the capsule of the liver; and (*c*) it finally breaks up between the lobules, supplying blood to the walls of the interlobular blood-vessels and the bile-ducts. Whether it transmits any blood directly to the lobule seems to be doubtful.

Within the lobule the capillary network is of the closest description, the capillaries being separated from one another by intervals commonly not larger than the diameter of two liver-cells. In the centre of each lobule the blood is collected into the central (*intralobular*) branches of the hepatic vein, which in turn collect and form larger branches (*sublobular*); these in turn merge into the large venous trunks of the hepatic vein, which finally opens into the inferior vena cava. Throughout their course the branches of the hepatic vein are distinguished by the thinness of their walls.

FUNCTIONS OF THE LIVER AND THEIR DISORDERS

Functions and the Disorders connected with them.

- i. Assimilative. (Glycogenetic, Proteolytic.)
- ii. Excretory.
  - (*a*) Water.
  - (*b*) Bile Pigments.
  - (*c*) Bile Salts.
  - (*d*) Cholesterin (Cholelithiasis).
  - (*e*) Drugs and Poisons (Jaundice and Biliousness).
- iii. Digestive.

Introduction.—Probably no organ of the body discharges functions at one and the same time so many, varied, and complex as the liver. It is at once a digestive organ, an important organ of excretion, and the chief assimilative organ in the body.

Its digestive and excretory functions are carried out through the agency of its secretion—the bile. The part played by this fluid in digestion is an extremely small one. It has no action on proteids or carbohydrates;

its only action is on fats, which it emulsifies and thereby facilitates their absorption.

On the other hand, as an organ of excretion the functions of the liver are of the highest importance. This excretory function is among the first to be called into requisition. Bile is formed as early as the third month of intra-uterine life, long before any necessity has arisen for digestive functions. The liver may be described as the excretory organ of the portal circulation, discharging the functions in relation to that circulation that the kidneys do in relation to the general circulation.

Its appearance in the animal scale is contemporaneous with the appearance of hæmoglobin in the body juices; and one of its chief functions throughout life, as it is one of its earliest, is to remove effete hæmoglobin from the body.

But its excretory functions are by no means confined to the pigments formed from hæmoglobin; they extend to the other products of proteid metabolism, some, like the bile acids, formed in the liver itself, others derived from the portal blood. Thus a large number of medicinal substances are excreted in the bile; while with regard to others not so excreted the liver exercises a function equally useful and effective, namely, that of destroying or modifying them. This function of the liver is probably of the utmost importance in protecting the body against a series of crude and more or less poisonous products formed during the process of digestion.

It is, however, in respect of nutrition that its functions are most varied and complex, and unfortunately still the most obscure. The liver elaborates and modifies nearly every product of digestion conveyed to it in the portal blood, acting not only on the primary products, such as peptones and sugar, but also on secondary products of amido-acid or aromatic nature, like leucin and tyrosin, or of basic nature, like lysine, lysatinine and ammonia, transforming them into urea, and possibly, in the case of the amido-acids, building them up again into more complex bodies.

The sum-total of this activity is evidenced by certain definite changes, among which the most notable are, first, the appearance of glycogen —followed later by its disappearance, the formation and excretion of bile acids in the bile, and the formation of urea.

It is convenient to speak of these as so many several processes; but it is important to bear in mind that they are probably all carried out in close connection with each other. At any rate, this is so in health. There is nevertheless a certain independence among the processes. Thus the formation of bile pigments and of bile acids, the two specific constituents of the bile, do not always go hand in hand, as was formerly thought. The bile pigments may be greatly increased (thus representing activity of the liver-cell in breaking up hæmoglobin) without any increase of bile acids (products of proteid metabolism). Indeed, the latter may be at the same time greatly diminished. As will afterwards be seen, this result is characteristic of most of the poisons that destroy the blood. They supply an increased amount of hæmoglobin to the liver wherewith to form bile pigments; but they appear rather to interfere with the general proteid metabolism on which the formation of bile acids depends.

The above summary of the various processes in the liver-cell may indicate in how many and various directions this element is open to functional disturbance which must affect the character of the blood and, indeed, nutrition generally.

The manner in which the liver-cell disposes of the products of its activity also calls for notice. While some of them return to the blood, others it no less invariably excretes into the bile, a fluid which is excreted at a low pressure along a long system of narrow passages, the lining epithelium of which is also excretory.

Both as regards the complexity of its processes, and the manner in which it gets rid of the products of its action, it is thus easily conceivable that disturbance of function may affect the bodily nutrition and health in many ways. To what extent it does so it is impossible within the limits of this article adequately to discuss. But some reference to the subject is necessary before entering on any consideration of disease of the liver, seeing that functional disorders of this organ bulk so largely in the minds of many persons as prominent factors in the causation of many diseases.

Three stages in our views of this matter may be distinguished.

For many centuries the liver was regarded as the chief organ of the vegetative processes within the body—the seat of sanguification and the centre of animal heat.

At a later period this view gave place to another, less general in character, which held sway during a period of two centuries. The chief function of the liver was held to be the secretion of bile, and all its disorders were discussed in relation to this function under the three heads of (*a*) diminished secretion, (*b*) increased secretion, (*c*) morbid secretion, that is, the secretion of morbid bile.

It is only with the information supplied by the researches of the present century, notably since the epoch-making discovery by Claude Bernard of its glycogenetic functions, that more extended and comprehensive views have been possible regarding other relations of functional disorder of the liver in disease. To no one are we more indebted for this result than to Murchison. In his well-known Croonian Lectures (1874) the first systematic attempt was made to give precision to the vague and indefinite views held on the subject, and to show that functional disorder of the liver may extend into other spheres and affect processes no less important to the organism than that of bile secretion—such processes, for example, as glycogenesis, the destructive metamorphosis of albuminoid matter generally, the formation of urea, and other nitrogenous products.

Murchison's views.—The classification Murchison proposed for such disorders was the following:—

α. *Abnormal nutrition.*—Both corpulence and emaciation may be the results of functional disorder, depending possibly on deficient formation of bile, with consequent defective assimilation of fatty and albuminous matters; or, on the other hand, on imperfect glycogenesis. The wasting of other diseases, such as phthisis or waxy disease, might also perhaps be referable to some functional disorder of the liver.

β. *Abnormal elimination.*—The disorders coming under this head are those connected with deficient elimination of bile; namely, costiveness, pale colour of stools, loss of appetite, furred tongue, bitter taste in the mouth, flatulence, sallowness of complexion, dingy conjunctivæ, languor and disinclination for work, frontal headache, dulness and heaviness, drowsiness after meals, great depression of spirits amounting occasionally to hypochondriasis, and lastly, frequent deposits of lithates in the urine. This group of symptoms might not unfitly be attributed to "torpor of the liver." The ensuing "engorgement of the liver" may well interfere with the normal processes of disintegration of albumin in the gland, and thus lead to the accumulation of deleterious products in the blood.

γ. *Abnormal disintegration* includes those disorders, probably the most important of all, due to imperfect disintegration of albuminous matters, and to the replacement of urea by other nitrogenous products.

The commonest example of this derangement Murchison conceived to be what he named "Lithuria,"—that is, the deposits in the urine of urates, uric acid, and pigmentary matters so commonly found in liver affections.

Symptoms of lithæmia.—Lithuria Murchison conceived to be as definite a disorder of liver function as glycosuria, and to be the result of abnormal albuminous disintegration and of a condition of blood ("lithæmia") induced thereby. This state of lithæmia, he said, may manifest itself in other ways than by the above-mentioned deposits; namely, by an extended train of symptoms, including a sense of weight and fulness in the epigastrium and region of the liver, flatulent distension of the stomach and bowels, heartburn and acid eructations, oppression and weariness, sleepiness after meals, bitter taste in the mouth, variable appetite, nausea, excessive secretion of viscid mucus in the fauces and at the back of the nose, furred tongue often large and indented at margins, constipation with scybalous motions sometimes dark at others clay-coloured, or diarrhœa, palpitation of the heart, irregularity or intermittence of pulse, frontal headache, restlessness at nights, bad dreams, and attacks of vertigo or dimness of sight often induced by particular articles of diet.

Lithæmia may manifest itself in gout, the foregoing train of symptoms being common in gouty people, and known as those of "gouty dyspepsia" or as "suppressed," "anomalous," or "latent" gout. In his opinion, articular gout is, so to speak, a local accident occurring in the midst of a train of phenomena due to abnormal albuminous disintegration within the liver. Gout, like diabetes, is in this case the result of functional derangement of the liver.

Lithæmia may also manifest itself by the formation of *urinary calculi.* Not only uric acid, which forms five-sixths of most urinary calculi, but also cystin, of which some are composed, are of hepatic origin. Xanthin also, and even oxalate of lime, are probably also connected with disorder of the liver, although evidence on this point is wanting. Anyhow, the symptoms of oxaluria closely resemble those of lithæmia as above described. In the great majority of cases of urinary calculi the liver is the organ primarily at fault.

As with urinary calculi, so also with *biliary calculi;* these also are frequently found in lithæmic persons, and are the result of functional derangement of the liver.

Another consequence and manifestation of this lithæmic dyscrasia may be *degeneration of the kidneys.* Murchison regarded lithæmia as the chief cause of acute nephritis; also of the granular, contracted, or gouty kidney; also of the degeneration of kidneys occurring as a sequel to diarrhœa; and lastly, of functional albuminuria, such as that connected with digestion, occurring independently of structural alterations.

Another consequence of lithæmia might be *structural diseases of the liver,* such as the fatty degeneration met with in alcoholics, catarrhal jaundice, some cases of cirrhosis, and, lastly, even primary cancer of the liver.

Other manifestations of lithæmia he conceived to be the *degenerations,* fatty and calcareous, met with in old age, and probably traceable to the functional inactivity of advancing years. When occurring earlier in life these degenerations are met with more often in those subject to lithæmia, in the gouty, for example, than in persons free from such tendencies.

Local inflammations are also favoured by the condition of lithæmia, persons of lithæmic habit being more prone than others to suffer from febrile colds and local inflammations generally.

Lastly, the lithæmic diathesis may influence the incidence and course of *constitutional diseases.* The liver is one of the organs that suffer most from the action of blood poisons, and at the same time contributes most to produce morbid states of the blood generally, such as diabetes or gout. Many constitutional diseases thus probably owe their origin to derangement of the liver. Among these he cited acute yellow atrophy of liver, erysipelas, pyæmia, acute rheumatism, tendency to thrombosis—a tendency especially well marked in tropical regions where hepatic derangements are so common (Fayrer)—deficiency of red corpuscles in anæmia, chlorosis, scrofula. Indeed, constitutional diseases generally he attributed in the first instance to some defective action of the liver.

The above summary will indicate both the character of the symptoms usually ascribed to disturbance of liver function, and also the wide sphere of influence it is possible to ascribe to functional liver disorder in the production of disease. Murchison's teaching represents, in my opinion, the extremest view it is possible to take of the importance of functional disorder of the liver in producing disease. The information gained since his views were originally put forth has thrown fresh light on many of the points he dealt with, and has necessitated some modifications of the above opinions.

In the present account I shall confine myself to the consideration of such facts as appear to throw fresh light on the subject; but the general outcome of my inquiry will be to show that in a large number of disorders assigned to the liver, the liver is as much the sufferer as the cause of suffering. Its disturbances, in a great majority of instances, arise not so much from any fault of its own, as from the fault of other organs connected with the portal circulation—to the presence of faulty products of digestion poured into the portal blood with which it has to deal. In another large group of cases the disturbances arise, not primarily in the liver-cell itself, but from morbid conditions in the bile passages, created (it may be) by the excretion of morbid products, whereby the due excretion of the bile is prevented.

I shall have to point out again and again that some of the chief hepatic disturbances—as, for example, biliousness, jaundice, diminished excretion of bile, cholelithiasis—are the result of changes, not in the liver-cell, but in the lining membrane of the bile passages; and that the disturbances of function of the liver-cell are consequences of these.

THE FUNCTIONS OF THE LIVER.—The functions of the liver may conveniently be considered under two headings:—

A. Assimilative. (Glycogenetic, Proteolytic, Metabolic.)

B. Biliary. { Excretory.
{ Digestive.

Under the word "Assimilative" I include not only glycogenesis, but also the whole series of important nutritive functions of which glycogenesis is but one feature; as the result of these functions proteid and carbohydrate materials are prepared and made assimilable for the tissues generally, while other derivatives of proteids are modified or built up into forms (urea) suitable for removal from the body.

A. Assimilative functions.—The disturbances connected with disorder of these functions may be dealt with briefly; not because of their small importance, but because we are in great ignorance of their nature.

Glycogenetic.—Thus with regard to glycogenesis, we know that the liver possesses a remarkable power of forming glycogen very easily from sugar; not only so, but also, in the absence of sugar, from ordinary proteid material. Glycogen accumulates in the cell during digestion, and in the intervals between meals disappears again; it is markedly increased on a diet rich in starchy food or sugar, but is not absent even when such food is withheld and proteids only are given; it is specially abundant in the liver of the healthy and well-nourished man; a suitable quantity of it seems essential for the efficient discharge of the many functions of the liver-cell; and either directly or indirectly it is thus essential to the nutrition of the body generally. We know further that the "glycogenetic" function of the liver is not an independent one carried out by the liver without relation to other processes within the liver-cell; for example, as I shall show later, the presence of glycogen greatly favours the destruction of hæmoglobin, and is most active when the supply of food material to the liver is greatest.

Nevertheless, while this is so, we know, both from experiment and from disease, that the function enjoys a certain independence; that, for example, certain drugs (phlorizin) possess the power of causing glycosuria, even in the starving animal, at a time when presumably the liver is free from glycogen, and no food material is reaching the liver; and, again, that in diabetes it seems to be affected to a special degree. It is thus easy to speculate that disturbance of this glycogenetic function may play an important part in disease; that in one case it may be responsible for leanness and wasting, while in another it may be responsible for the opposite effect of corpulence. But such speculations do not carry us far. In the absence of more precise information as to the nature of the disturbance, they are only other ways of saying that in the one case there is malnutrition and wasting, while in the other nutrition is good. Even if some disturbance there be, there is no evidence that it is the primary one, that it is not a concurrent effect of some change affecting the organs of nutrition and the tissues generally, and not the liver especially.

Apart then from its effects on nutrition, we know little definite with regard to disturbances of this hepatic function in disease. That it is gravely affected in many conditions of disease is certain; but, with the exception of diabetes, it is probable that altered glycogenetic activity is only one expression of a general disturbance affecting the general activity of the liver-cell in relation to nutrition. I say especially "in relation to nutrition," for I shall have to point out later that the excretory activity of the liver may be unaffected, while its nutritive activity, judged by the formation of glycogen and the formation of bile acids, is in abeyance.

Thus, as will presently be seen, poisons may induce a greatly increased formation of bile pigments by the liver, while the bile acids are reduced to a minimum, and no trace of glycogen is discoverable. Similarly in disease, the power of forming bile is retained by the liver to the very last, long after the power of forming glycogen may have been lost.

Proteolytic.—With regard to the other functions of the liver in relation to nutrition, the breaking up of proteid material, the dealing with the various secondary products, whether formed within itself (for example, glycocine), absorbed from the intestine (for example, leucin and tyrosin), or conveyed to it from the tissues generally, we know that grave disturbances also occur in disease.

Urea represents the chief form in which the waste nitrogen is removed from the body. All evidence goes to show that it is formed within the liver by synthesis from ammonia; and that uric acid (a combination of glycocine and urea) probably represents a product of a metabolism within the liver-cell slightly divergent from that leading to urea. In rare cases, again, where the liver-cell undergoes rapid destruction (as in acute yellow atrophy), urea may almost disappear, and its place be taken by products such as leucin and tyrosin, which, ordinarily, are duly arrested and broken up by the liver. We know further that this last extreme is producible by the action of certain poisons on the liver-cell (for example, phosphorus), precisely as we saw that the glycogenetic function could be specially affected by other poisons (phlorizin), or the bile-forming function by others again (toluylendiamin).

It is thus extremely probable that in disease these particular activities may be gravely affected, and that in this way disturbances in nutrition and metabolism may be produced. Indications that this is the case we often obtain, indeed, from the urine, in the changed character or quantity of the colouring matters; in the increase of urates or uric acid; in increase of ammonia at the expense of urea. But beyond this we know little. We do not know to what extent these disturbances of functions are themselves the primary or chief disorder, or, on the other hand, are but the effects of morbid change elsewhere. Thus for the large group of cases included by Murchison under the title of "lithæmia," and regarded by him as in a special degree the result of functional disorder of the liver, I shall presently have to show that the functional disturbances which undoubtedly do occur are not the primary, and may not be even the most important; that in all probability they are really secondary to disturbances initiated elsewhere, perhaps in the gastro-intestinal area.

Further, I have now to show that increase of uric acid and urates may be an evidence of changes in lymph-forming structures, rather than in the liver.

Thus with regard to the assumed connection between increase of uric acid and of urates in the urine and liver disturbance, some modification of our views is rendered necessary in the light of recent knowledge. For certain observations indicate that uric acid may have more than one origin in the body—not merely by synthesis of urea and glycocine in the liver (or kidney, Luff), but independently of the liver from the nuclein constituent of cells generally, especially lymphatic cells. Hence they suggest that in certain cases increase of urates and uric acid may represent a disorder of the blood rather than of the liver itself. There is found to be a parallelism between the excretion of uric acid and the number of leucocytes in the blood; increase of leucocytes after food is accompanied by an increased excretion of uric acid; diminution of the leucocytes during inanition by a diminished excretion. Quinine, which reduces the number of leucocytes, diminishes the excretion of uric acid; pilocarpine, which causes a decided increase of leucocytes, increases the uric acid. This connection between leucocytosis and uric acid excretion is, however, best shown in leucocythæmia. The excretion of uric acid in this disease is notably increased, sometimes more than doubled; the source of the uric acid in these cases has been shown to be nuclein—the substance which forces the main constituent of the nuclear part of cell. Again, the administration of nucleins causes an increased excretion of uric acid. According to Horbaczewski, the chief seat of origin is the lymphatic elements of the spleen; though it likewise appears that all organs of the body contain substances, of the nature of nucleins, capable under given conditions of being split up into uric acid, but none so richly as the spleen. It is probable that the increase of uric acid which rapidly occurs after digestion of food is directly related to the increased activity of the leucocytes of the blood and lymphatic elements, generally both in the spleen and the gastro-intestinal mucosa, which always occurs at this period. This leucocytosis is noticeable as early as one hour after digestion, and reaches its maximum about the third hour, after which time it falls; sometimes more quickly, sometimes more slowly. The increase varies from 36 per cent to as much as 146 per cent; the average of fifty observations was 78 per cent (Pohl). The rise in the uric acid excretion is related to this increase of leucocytes, not merely to the food taken; for in those exceptional cases in which no leucocytosis occurs after digestion of food, the increase in uric acid is also wanting. The increase of urates and uric acid in the urine may thus denote functional disturbance of lymphatic structures rather than disturbance of liver function.

B. Biliary functions.—1. Excretory functions.—*The Bile.*—Normal bile is a somewhat viscous fluid of a golden yellow or olive-green colour, faintly alkaline reaction, sweet bitter taste, and mean specific gravity about 1008. Its average daily quantity is about 1 to 1½ pint, containing about 1½ to 2 per cent of solids. Its chief constituents are:—(i.) Bile pigments: bilirubin, biliverdin. (ii.) Bile salts: glycocholate and taurocholate of soda. (iii.) Mucus, derived from bile passages and gall-bladder, formerly thought to consist of mucin, but now known to be more complex —a mucoid nucleo-albumin. (iv.) Cholesterin: ("Bile fat"). (v.) Fats: palmitin, stearin, and olein. Soaps: alkaline salts of palmitic, stearic, and oleic acids. (vi.) Lecithin or products derived from its decomposition. (vii.) Inorganic salts: about 0·8 per cent, consisting chiefly of chloride of sodium and phosphate of sodium, with smaller traces of carbonate of soda, phosphate of iron, phosphate of lime.

Conditions influencing the amount of bile.—The secretion of bile is probably continuous, though varying in activity from time to time. Its discharge into the duodenum, however, is intermittent, and takes place chiefly in relation to digestion. It does not flow continuously, but is expelled from time to time, in a series of jerks, by the peristaltic contractions of the walls of bile-ducts and gall-bladder. The walls of the bile-ducts, even to their smaller branches, are richly supplied with unstriped muscular fibres, both circular and longitudinal. The conditions influencing the character and flow of bile have been chiefly studied in dogs with biliary fistula. Opportunities for such studies in man rarely present themselves; of late years some valuable observations in such cases have been recorded by Copeman and Winston (1889), Mayo Robson (1890), Noel Paton and Balfour (1891), and Noel Paton (1892). These observations show that the amount of bile secreted varies greatly under the influence of many different factors—most of them being still obscure. Throughout the twenty-four hours its flow is irregular, but in general it is highest about the middle of the day (12-4), and lowest in the early hours of the morning. Taking food is undoubtedly the chief factor which influences its flow in health; the flow of bile increases when food is taken, and falls when food is withheld. But even the influence of food is not an immediate one, for the largest amount of solids is not excreted when digestion is actively going on, but subsequently, when presumably the liver is dealing with the products absorbed.

The flow of bile is greatly influenced by the amount of fluid taken, and this probably accounts for the increased flow during the day. But this excretion of water is no mere mechanical filtration; the pressure at which the bile is secreted is several times higher than that of the portal blood from which the water is obtained. The amount of water excreted is thus primarily dependent upon the activity of the liver-cells, not upon the amount of water in the blood. The injection of water directly into the blood, or its administration by the mouth or rectum, does not necessarily cause any increased flow; indeed, according to Stadelmann, it has no influence upon it at all. But notwithstanding these experimental results, there can be no doubt that increased consumption of water, if not directly by its mere presence in the blood, then indirectly by the products which it carries with it in increased quantity from the intestines and tissues, has a notable effect on the amount of bile excreted. And it is this flushing of the biliary system with water which serves to explain the remarkably beneficial action of the larger number of the mineral springs. That the excretion of water is influenced by the activity of the liver-cell, rather than by mere amount of water, is shown by the fact that while large quantities of water administered by the mouth may have little or no apparent effect, the administration of food, or still more markedly the introduction of bile into the intestine, is always followed by an increased flow. No product absorbed from the intestine seems to have so remarkable a stimulating action on the liver-cell as its own bile salts.

Influence of Drugs.—Among drugs found by Prevost and Binet to possess any power of increasing the flow of bile in dogs with biliary fistulæ, were turpentine, chlorate of potash, benzoate and salicylate of soda, salol, euonymin, and muscarin; none of these, however, was so powerful in this respect as the bile or bile salts.

The following were found weak and uncertain in their action: bicarbonate of soda, sulphate of soda, chloride of sodium, Carlsbad salts, antipyrin, aloes, rhubarb, ipecacuanha, hydrastis Canadensis.

The flow was diminished by calomel, iodide of potassium, iron, copper, atropin, and strychnine.

It was quite unaffected by phosphate of soda, bromide of potassium, arseniate of soda, corrosive sublimate, alcohol, ether, glycerine, quinine, caffeine, pilocarpin.

Nissen (1890), who carried out a similar investigation, found that alkalies like bicarbonate of soda, *chloride of sodium, sulphate of soda*, Carlsbad salts, acetate of potash, sulphate of potash, salicylate of soda, in small doses were without influence, while in stronger doses they caused a diminution; bile and bile salts, on the other hand, caused an increase both of bile and the bile salts, but no increase of bile pigment. With regard to one of the above salts—salicylate of soda—a consensus of opinion is against Nissen's result. Thus Rosenberg (1889) found that in doses of fifteen to thirty grains it caused an increased flow with diminished consistence. Lewaschew (1884) found that it caused a notable increase (more than double), while the solids were reduced to less than one-third their former amount; it had indeed a more intense influence on the amount (and character) of bile than any other alkali.

This result agrees with that obtained by Professor Rutherford, to whose well-known researches we are indebted originally for most of our knowledge regarding the action of drugs on the amount of bile. He found salicylate (as also benzoate) of soda to be eminent examples of pure "hepatic stimulants," that is, of stimulants acting on the liver and not on the intestinal glands. In their case of biliary fistula Noel Paton and Balfour were able to confirm this conclusion, for they found that administration of salicylate of soda caused an increase of bile from 492 c.c. to 580 c.c.

The drugs found by Rutherford to increase the flow of bile were sodium phosphate, mercuric chloride, ipecacuanha, colchicum, jalap, aloes, colocynth; rhubarb and dilute nitro-hydrochloric acid were also found to be hepatic stimulants, but much feebler in their action. Calomel he found to stimulate the intestinal glands, but not the liver. Drugs, like magnesium sulphate, gamboge, and castor oil, which acted as purgatives diminished the secretion of bile.

Other drugs, the action of which on the flow of bile has been studied, are olive oil and Durand's remedy (oil of turpentine and ether). Rosenberg (1889), experimenting on a dog with biliary fistula, found that 50 to 120 grammes of olive oil by the mouth always caused within thirty to forty-five minutes a considerable increase of bile with diminished consistence; whereas bile always caused an increased secretion with increased consistence. Durand's remedy caused a slight increase due to the turpentine (ether had no effect). Carlsbad salts, given in gelatine capsules, diminished the secretion and were without cholagogue action. The best cholagogue, next to the bile itself, he considered to be olive oil.

Some valuable observations were made by Mr. Mayo Robson in his case of biliary fistula. On different occasions he administered calomel (gr. v.), euonymin (gr. iv.), rhubarb (℥ss. and ʒj. of tincture), podophyllin, iridin (gr. iv.), turpentine (♏xv. in capsule), aerated soda water and benzoate of soda. The only two of these that had any cholagogic action were aerated soda water, which produced a distinct increase maintained for some time, and iridin, which increased the flow temporarily, without however augmenting the total quantity in twenty-four hours.

The other drugs seemed rather to diminish the flow of bile than to increase it.

The most recent observations on this subject, carried out by various pupils of Stadelmann (1890-92), also throw doubt upon the existence of so-called cholagogue drugs. Thus Glass (1892) tested the action of bicarbonate of soda, chloride of sodium, sulphate of soda, and artificial Carlsbad salts on a dog with biliary fistula, and failed to find any cholagogue action. None of these drugs passed into the bile or increased its alkalinity.

The whole tendency of later observations appears thus to cast doubt on the existence of any drugs possessing the power of stimulating the liver directly to increased secretion of bile; and some observers have gone as far as to assert that cholagogues do not exist (Neumeister, 1893). This view is not shared by Gamgee, who considers that judgment should be withheld until further observations are made. With this view of Gamgee I am disposed to concur. Although the action of many of the agents above considered has been overrated, and powers ascribed to them in this respect which they do not possess, there appears to me to be no sufficient ground for doubting the existence of drugs capable of influencing the action of the liver-cell directly. The strongest argument to the contrary is that the bile salts certainly possess such a power to a remarkable degree. Their administration, or that of bile, always occasions an increased flow of bile as well as an increase in the solids. Among the drugs mentioned above, the one for which some similar power appears to be most fully ascertained is salicylate of soda. All observers, excepting Nissen, have found it to cause an increase of the bile.

The whole subject, however, is one of great complexity. As Professor Rutherford has well pointed out, it is impossible to ascertain the factors which bring about an increase of the bile in the stools after administration of a particular drug. The factor may be (α) stimulation of the hepatic secreting apparatus; (β) the stimulation of the muscular fibres of the gall-bladder and larger bile-ducts, that is, the bile-expelling apparatus; (γ) the removal of a catarrhal or congested state of the orifice of the common bile-duct, or of the general extent of the larger bile-ducts; (δ) the removal from the intestines of substances which had been passing into the portal vein and depressing the action of the hepatic cells; (ϵ) or the stimulation of the intestinal glands, which drains the portal system, and relieves the "loaded" liver. To these I would add as another possible factor (ζ) the stimulation not merely of the intestinal glands, but of the whole mass of lymph-cells in the mucosa of the intestine, and of the cells of the spleen, the action of which, according to my observations, is so important in determining both the character of the products carried forward to the liver and the constitution of the blood itself. Inactivity of this mass of cells, by allowing injurious products to reach the liver, may be the chief factor responsible for inefficient activity of the liver and deficient flow of bile. Drugs which influence the action of this group of cells may thus affect the flow of bile, not directly in virtue of any special action on the liver-cell, but indirectly through their action on these other tissues.

Until, then, our information concerning the mode of action of such drugs on biliary secretion be more definite, I think it would be better not to apply the title of "hepatic stimulant" to them so freely as is sometimes done, not to speak as if the whole force of their action fell on the liver-cell, whereas it is possible, as above indicated, that many other factors may be at work. And if, as is convenient, the name cholagogue be applied to them, it should be with the distinct reservation that we are still ignorant of the part played by the liver-cell itself, by the expelling apparatus, and, lastly, by the tissues outside the liver—notably those of intestinal mucosa and spleen—respectively in the production of the increased flow of bile.

Conclusion.—To sum up the influences causing an increase in the quantity of bile, the three chief' are increased supply of water, the absorption of bile or bile salts, and the absorption of the food products.

The action of water is not a direct one; mere wateriness of blood—produced, for example, by injection of water directly into the blood—does not cause an increased flow of bile. So that its effect in increasing the flow when administered by the mouth or by the intestine is probably due to products washed out from the intestinal walls and carried to the liver. To get the full effect of this action of water in diluting the bile, care should be taken not to give the water with the food. Food alone causes an increased flow of bile; for instance, the most copious flow is during the day, and a fall takes place during the night; nevertheless it is during the night that the bile is richest in solids. If, then, our object be to increase the fluidity of bile, that object is best attained by giving water when the natural tendency is for the bile to become more concentrated, that is, either between meals or at night time several hours after the last meal. As a matter of clinical experience I have found this practice yield the best possible results; for example, in cases of jaundice due apparently to highly concentrated bile and "biliary sand" in the bile-ducts.

So far as drugs are concerned, some few (salicylate of soda, benzoate of soda, turpentine, olive oil) seem to possess the power of exciting an increased flow of bile; but the action of most other so-called "cholagogues" is uncertain, and, even in the case of those above mentioned, their mode of action is quite undetermined.

So far I have had under consideration the various agents capable of exciting an increased flow of bile. For it is to combat successfully the conditions which lessen the flow of bile that our chief efforts are directed in disease.

Diminished flow of bile.—Some interesting information regarding the mechanism underlying bile secretion is obtainable from a study of the factors concerned in reducing the quantity of bile; and to these I must now draw attention.

Influence of fever.—All observers are agreed that fever diminishes the secretion of bile. Thus in a case of a biliary fistula recorded by Eiffelmann it was noticed that on the onset of pneumonia, and again of an attack of dysentery, the flow of bile ceased. In the case recorded by Paton and Balfour the patient suffered from time to time from feverish attacks, and this condition had the most distinct effect upon the amount of bile excreted. During the 11 days of the first attack the amount fell from an average of 650 c.c. a day to 475 c.c., while the solids fell from 8 and 9 grammes to 3·7 grammes. The subsequent restoration to the normal was slow. In a second attack, on a rise of temperature to 99·6° F., the bile fell from 592 c.c. to 238 c.c., and the solids from 9·2 to 3·2 grammes.

These observations agree with the experimental results obtained by Pisenti (1886), who finds that fever invariably causes a diminution in the excretion of bile—the diminution being one-third to one-half the normal. This diminished excretion of water appears to be the result of fever itself, irrespective of its nature; the diminution in the amount of solids, on the other hand, appears to depend upon the nature of the fever. Moreover, in fever the bile always contains a larger amount of mucin; and the colouring matters seem also to undergo alteration, the bile becoming much darker, almost black; sometimes of a dark green colour. All these changes are purely functional, as examination of the liver failed to reveal any organic change.

In the case of Noel Paton and Balfour, a noteworthy change in the bile was that during attacks of fever the excretion always became markedly paler, and on several occasions was quite colourless.

Influence of Poison.—A varying and sometimes notable concentration of bile has been shown by Stadelmann to be one of the chief features of the action of hæmolytic poisons generally. Thus, after injection of hæmoglobin, for the first ten hours there is no obvious change in the bile; then the quantity falls, and the bile becomes thicker, more concentrated, and very dark in colour: this variation continues for twenty-four hours, the bile being reduced to one-third its normal amount. (At the same time the bile pigments are greatly increased by as much as 56 per cent, the bile acids being diminished by about the same amount.)

Toluylendiamin—a drug possessing marked hæmolytic and icterogenetic properties—causes similar changes. In the first stage, lasting about twelve hours, the bile is increased in quantity (and is very rich in pigments); then follows a second stage, during which it appears to lose all the characters of bile, and is replaced by a small quantity of extremely viscid colourless mucus. After sixty to seventy hours the bile gradually regains its normal character.

Phosphorus also is found to act similarly; at first it causes an increase of bile; the bile then falls to one-fifth of its former amount, and becomes clearer and more mucoid.

The action of arseniuretted hydrogen is also attended with a remarkable concentration of bile, the gall-bladder and bile-ducts being filled with thick viscid bile, which frequently contains large quantities of amorphous sediment as well as numerous crystals of bilirubin. The bile is reduced to as much as one-fifth its former amount (while the bile pigments are increased to as much as 3½ times, and the bile acids are diminished to as much as one-tenth of their former amount).

The importance of these observations in connection with the jaundice produced by poison I shall discuss fully elsewhere (art. "Jaundice").

These observations have, however, an importance in relation to the whole of the class of liver disorders attended with a diminished flow of bile—for no factor is more important in producing functional liver disorders than this of diminished secretion of bile. The troubles it occasions arise not so much from diminution of the output of the specific constituents of the bile—the bile pigments and bile acids—for the former, indeed, are usually much increased while the latter are usually even more markedly diminished, as from the temporary stagnation of bile which gives opportunity for the absorption of its constituents, and reacting on the liver-cell disturbs its function.

What, then, is the cause of this diminished flow? Is it the result of a specific action of the poison on the hepatic cell, whereby its excretory function is temporarily arrested? That the action is in some degree specific seems to be indicated by the remarkable difference in the behaviour of the chief bile constituents; the bile pigments are usually notably increased, thus indicating great activity of the liver-cell in taking up and destroying the hæmoglobin conveyed to it, while the bile acids on the other hand are no less remarkably diminished, indicating a lessened proteid metabolism within the cell.

It is possible that by the direct action of a poison the excretion of water may be temporarily lessened. The concentration of the bile in such cases may then be due in part to a lessened aqueous excretion on the part of the hepatic cell. But the chief cause underlying it I believe to be an increased formation of mucus by the epithelium lining the bile passages. The action of the poison is not limited to the hepatic cell, but extends to the lining of the bile passages. As we shall presently see, the bile is an important channel for the excretion of poisons and drugs present in the blood; and it is the excretion of such more or less irritant products that is apt to excite catarrh of the bile passages, increased secretion of mucus, and consequent increased viscidity of bile.

If the excreted products be harmless, their passage along the bile-ducts is without ill effect on the lining epithelium. If, however, they possess any irritant properties they will tend to excite increased secretion of mucus, not only from the mucous glands of the larger bile-ducts and the gall-bladder, but from the epithelium of the smaller bile passages; and in proportion to their irritant character and the resulting increase of mucus will be the tendency for the flow of bile, excreted under very low pressure at all times, to be retarded, and for the bile thus to become more concentrated.

Such, briefly, I consider to be the way in which the amount of bile can be diminished by changes in the bile passages. Under ordinary circumstances the only effect is to favour and promote absorption of its water as it passes along them. If it pass a certain degree, however, some of its bile constituents may also be absorbed; and thus arises the slight icterus of the conjunctivæ (from absorption of some bile pigment) characteristic of the condition termed "biliousness."

If the conditions underlying these changes persist or frequently recur, then the ill effects of diminished wateriness of bile extends beyond the production of mere "biliousness." Repeated irritation of the lining of the bile passages by such products tends to promote a chronic tendency in the bile passages and in the gall-bladder (where the bile rests for some time and becomes more concentrated) to catarrh. The basis is thus laid not only for more or less chronic biliousness, but also for the production of some of the chief changes in the bile which underlie the formation of gall-stones; these are stagnation of bile, increased formation of cholesterin by the epithelium of the bile passages, precipitation of bilirubin-calcium, and presence of inspissated mucus.

Summary.—Our consideration of the chief conditions influencing the amount of water in the bile has thus led to some important conclusions.

1. There is no evidence that any disturbance ever arises from too great an excretion of water in the bile, if indeed such dilution ever takes place.

Older writers recognised the existence of a "polycholia"—an increased flow of bile—and were disposed to attribute certain ill effects to it,—notably an increased absorption of bile pigment from the intestine and the production thereby of a form of jaundice (Frerichs). As I shall show later (art. "Jaundice," p. 74), the origin of a jaundice in this way is exceedingly doubtful. It is true one important form of jaundice—that connected with blood disorder and increased destruction of hæmoglobin—is frequently associated with an increased flow of bile rich in colouring matters. The essential change of the bile in such cases is, however, not increase in its quantity, but increase in its pigments. It is not a polycholia, which is a name only rightly applicable to an increase of all the bile constituents, but a polychromia; and the jaundice so frequently associated with this change is due, not to increased absorption of bile from the intestine, but to absorption from the bile passages as the result of increased viscidity. So far from any aqueous dilution ever being a cause of disturbance, it is the one condition of bile which all our efforts are directed to produce; and the task is by no means easy.

2. On the contrary, one of the most potent factors in hepatic derangement is diminished fluidity with lessened flow of bile. This may be the outcome of defective excretion on the part of the liver-cell; and such is probably its character in fever, in which the amount of bile is always diminished.

But another and, in my opinion, more common and potent factor is increase of resistance to its flow (at all times under very low pressure) along the bile passages. This increased resistance may arise from one of two sources: either from sluggish peristaltic action of the walls of the bile-ducts (and gall-bladder?), one of the most important factors in the passage of bile from the bile-ducts; or from increased secretion of mucus, and corresponding abnormal viscidity of bile.

Both these conditions, but more especially the latter, underlie the state of "biliousness"; and the increase of mucus is the result of the irritant action of products excreted in the bile. For the formation of these products in the first instance the liver may not be in any way responsible: they have been formed elsewhere; they reach it in the portal blood, and it has duly excreted them. Were it not for their irritant action on the bile passages in the course of their excretion, few or no ill effects might be produced. But the increased formation of mucus excited by their action as they pass along the bile passages has as its result an increased viscidity of bile—a retardation of its flow and a diminution of its quantity.

Whether, then, the diminution of bile be caused directly by impaired action of the liver-cell, or indirectly by increased resistance in the bile passages, it is important to note that the primary cause of the mischief is not necessarily the liver itself. The disorder is set up by products conveyed to it in the portal blood. Thus all agents which promote healthy action of the gastric and intestinal mucosa may, by preventing the formation and absorption of abnormal and possibly irritant products, and by freeing the liver and its bile passages from their injurious presence, promote an increased flow of bile, and thus indirectly have a cholagogue action.

Excretion of bile pigments.—The bile acids and the bile pigments are the two specific constituents of the bile. Owing to their remarkable staining power, the pigments are the most conspicuous of the constituents; hence their behaviour in disease has always attracted a special amount of interest. Their presence in the blood and tissues constitutes jaundice; and no symptom connected with liver disturbance is so prominent or has excited so much attention as this. The source of these bile pigments, the conditions influencing their amount, the variations, quantitative and qualitative, to which they are subject in disease, the factors determining their presence in the blood and tissues, have thus an exceptional interest for the physician. The formation of bile pigment is one of the first functions discharged by the liver in intra-uterine life. Bile pigment begins to be formed and to be excreted as early as the third month of intra-uterine life, before there is any necessity for digestive juices, even before there is any evidence of a glycogenetic function on the part of the liver. The meconium present in the intestine at birth is made up of bile pigment—without a trace, as it is interesting to note in passing, of any reduction products like hydrobilirubin (stercobilin), which constitute the chief colouring matters of the fæces in extra-uterine life. As it is one of the first functions to appear, so pigment formation is one of the last to disappear. Throughout life the formation and excretion of bile pigment continue to be the most persistent function of the liver.

The two chief bile pigments are bilirubin and biliverdin. It has been customary to regard the former as the more important of the two; but we may note that Mayo Robson, and Copeman and Winstow, who have had opportunities for studying the bile in cases of biliary fistula, agree in the opinion that biliverdin is the more important. The main point with regard to their formation is that they do not exist preformed in the blood: they are not merely excreted by the liver; they are both formed and excreted by this organ.

The question of the possible extrahepatic (hæmatogenous) origin of bile pigment, which has played so prominent a part in the discussions on the origin of certain forms of jaundice, is, in my opinion, finally answered (see art. "Jaundice," p. 57). The formation of bile pigment is a purely hepatic function discharged by the liver-cell itself. It is stopped by removal of the liver.

Bile pigment, then, is formed from hæmoglobin within the liver itself, and is excreted thence into the bile. It is the chief mode in which the pigment element of hæmoglobin is excreted from the body. Thus the mode of its formation has a special significance in relation to the ultimate fate of hæmoglobin. The appearance of hæmoglobin in the scale of animal development, and the appearance of an organ like the liver, are contemporaneous. It would thus appear that there is a certain wear and tear of the hæmoglobin in the discharge of its important functions in the blood; and that this necessitates its destruction and removal from the body. This removal the liver effects; it breaks up the hæmoglobin, excreting one part of it in the form of bile pigment, but retaining within itself most of the important element—the iron—probably for further use.

The relation of the bile pigment to hæmoglobin may thus be compared with that of urea to proteid material generally; it is the form in which a waste product is removed from the body. It is a purely waste product: it subserves no function; and, according to Bouchard, whose observations, however, on this point have not been confirmed, it is not only a waste product but also a poisonous one.

Whatsoever interest, then, may attach to it is connected with its relationship to hæmoglobin on the one hand, as an index of the amount of hæmoglobin daily broken up and renewed, and with its relationship to the liver-cell on the other, as an index of its activity.

The liver as a hæmolytic organ.—It is in virtue of the undoubted derivation of bile pigment from hæmoglobin that the liver is usually regarded as the most important seat of hæmolysis within the body. Certainly no organ has so much to do with getting rid of hæmoglobin set free within the blood as the liver. But there is, I think, some confusion in this matter. By hæmolysis I mean those series of changes in the blood—in its plasma, leucocytes, and red corpuscles—which tend to their disintegration. In the case of the red corpuscle such changes result in the liberation of the hæmoglobin; but the place where this liberation occurs is not necessarily the place where the hæmoglobin is ultimately broken up and disposed of. My investigations on this point indicate that such hæmolytic change in health occurs almost exclusively within the portal blood system. But this hæmolysis is by no means confined or even mainly confined to the liver. According to my observations, the spleen and the mass of capillaries in the mucosa of the intestinal canal are even more important seats of this change than the liver. Increased hæmolysis is a periodic event coincident with the digestion of the food products, and caused by the activity of the mass of cells concerned in absorbing these products. It may be increased by the action of drugs, which set free more hæmoglobin; but even drugs only act indirectly by stimulating activity of the cells in closest relation in the blood—especially those of the spleen and the gastro-intestinal mucosa. Thus I found with toluylendiamin, a drug possessing a marked hæmolytic action, that removal of the spleen markedly lessens its destructive action. If this drug be injected directly into the blood of rabbits from which the spleen has been previously removed, its destructive action is reduced by more than one-half; indeed, the action of moderate doses is destroyed. The spleen then, more than any other organ, seems to be concerned in the hæmolysis caused by this drug; although, judging from the evidences of its action on the liver when injected into the healthy animal, namely, the increase of bile pigment and deposit of iron in the liver-cells, the liver rather than the spleen would have appeared to be the chief seat of the hæmolysis. Complete removal of the spleen, however, arrested all such changes, notwithstanding the injection of double the dose of the drug.

As the result of these investigations, then, I find myself unable to regard the liver as the most important organ concerned in hæmolysis. It is hardly possible, indeed, to doubt that hæmolytic changes consequent on the activity of its cells do occur in its capillaries. But these, in my opinion, are less important than those which go on within the spleen, where the blood is brought most closely into relation with active cells; and are even less than those which go on in the mass of capillaries in the gastro-intestinal mucosa. I consider that the chief function of the liver in relation to hæmolysis is to arrest and get rid of the products of hæmolysis conveyed to it in the portal blood from the spleen and intestines; and the most prominent of these products is hæmoglobin.

It is important to bear these distinctions in mind. For it will then be clear that increased formation of bile pigment, if rightly regarded, affords not only an index to the activity of the liver-cell in breaking up hæmoglobin, but to a certain extent is also an index of the activity of the spleen and the cells of the gastro-intestinal mucosa, which parts are chiefly concerned in liberating hæmoglobin.

Deficient formation of bile pigment may thus have as its cause, not inactivity of the liver, but a lessened hæmolysis due to inactivity of the other organs in relation to the portal blood. Conversely, increased formation of bile pigment must always have been preceded by an increased hæmolysis, denoting increased activity of organs other than the liver. Thus to say of a drug, which induces an increased formation of bile pigment, that it has "stimulated the liver to increased secretion," by no means embodies all the truth in respect of the manner in which this increased secretion is produced. It has not only stimulated the liver, but it has also stimulated the other organs of the portal circulation responsible for the preceding hæmolysis. Thus with regard to one of its most specific functions—the formation of bile pigments, the point is brought out that the liver is dealing with hæmoglobin liberated mainly elsewhere, and conveyed to it in the portal blood. Deficient formation of bile pigment—which, on the view that the liver is alone responsible for hæmolysis, would be peculiarly a symptom of "sluggish liver"—implies, then, sluggishness of organs other than the liver.

Passing from these general considerations to the variations met with in health and disease, I have to note that the actual amount of bile pigment which gives its colour to the bile is very small, though its staining powers are very high. The daily excretion in health, though differing in different individuals, is probably fairly uniform. In general the variations that occur seem closely to follow the variations in the other solid constituents. They are increased by food, diminished when food is withheld.

Polychromia and its relation to jaundice.—For the information we possess as to the variations that occur in disease, we are indebted mainly to observation of the pigments present in the urine; but we have also a few observations made directly. Thus a large increase always follows the injection of hæmoglobin into the blood, or again, of hæmolytic agents that set free hæmoglobin; such as distilled water, toluylendiamin, and arseniuretted hydrogen (Stadelmann). This increase may run as high as three to four times the normal amount. It usually makes itself manifest in from 3 to 4 hours after the injection of the hæmoglobin. If the injection be merely subcutaneous it is later—12-14 hours. This "polychromia," as it has been named by Stadelmann, is not necessarily accompanied by an increase of bile; on the contrary, the bile is generally diminished in quantity and highly concentrated—sometimes to a notable degree. Even more remarkable is the behaviour of the bile acids; instead of being increased, they are reduced to mere traces. Great activity of the liver-cell in one direction (formation of bile pigment) is thus compatible with lessened activity in others (excretion of water, formation of bile acids). These observations are of special interest in regard to the bile acids. Absence of bile acids has usually been regarded as an important evidence of inaction of the liver; and hence came the notion that jaundice without bile acids in the urine denotes that the bile pigment must have been formed elsewhere than in the liver ("hæmatogenous jaundice"). It is now made clear that no such significance attaches to the absence of bile acids; their defect is quite compatible with a greatly increased formation of bile pigments by the liver. A similar increase of bile pigments is a feature common to all conditions in which blood-destruction is increased. According to my observations, it is a constant and most notable feature of the bile in pernicious anæmia; in no morbid state does the bile possess such extraordinary staining power as in this disease. An increase of bile pigments likewise attends the absorption of large extravasations of blood, and is a feature also of most of the forms of jaundice caused by poisons.

It is in relation to jaundice that the chief interest has hitherto attached to this increase of bile pigments. The occurrence of jaundice in association with excess of bile in the stools has long been noticed; it constitutes the "jaundice from polycholia" of old writers. The doctrine taught by Frerichs was that the jaundice in such cases is due to excess of bile pigments, their increased absorption from the intestine, and their deficient disintegration in the blood. The later form of this teaching is that bile pigments are absorbed in such excess that the liver is unable to excrete them all, so that some escape through the liver into the general circulation and produce the jaundice. These doctrines I shall discuss more fully elsewhere (*vide* art. "Jaundice," p. 74). At present I will only say that, in my opinion, there is no sufficient evidence that jaundice ever arises in this way. Some bile pigment is probably always absorbed from the intestine to be excreted again in the bile; but the extent to which such an absorption occurs is doubtful, and in all probability has been much exaggerated. It may be regarded as certain, however, that any pigment so absorbed is excreted again, for the liver rapidly takes up and excretes any bile pigment present in the blood. Thus bilirubin injected directly into the blood is entirely excreted through the bile in from two to four hours after its injection. Similarly the increase of bile pigments following injection of bile into the duodenum, as shown by Schiff and Rutherford, is always greater when bile is introduced than when a corresponding amount of bile salts are so introduced.

In the absence, then, of any other explanation of the jaundice with polycholia, we might attribute it to an increase of this absorption—of this "circulation of bile pigment." But Stadelmann's observations show that drugs which cause polychromia usually cause other changes in the bile—one of the most notable being that at one time or other there is a remarkable increase in its viscidity, leading sometimes to arrest of its flow. This arrest it is that causes the jaundice. The jaundice results from absorption of bile from the bile-ducts, not from the intestine. Both preceding and following this stage of increased viscidity there is a greatly increased excretion of bile pigments; hence the abundance of bile pigment in the intestines, so frequently noted in these cases. The "jaundice of polycholia" is thus hepatogenous (obstructive), and is not due to an increased absorption from the intestine.

Excretion of hæmoglobin into the bile.—I have now to point out, with regard to this action of the liver on hæmoglobin, that it is not simply a question of mere amount—of so much free hæmoglobin in the blood, with resulting formation of so much bile pigment. Increase of bile pigments is not necessarily proportionate to the amount of free hæmoglobin in the blood. Thus the injection of distilled water or pyrogallic acid produces intense hæmoglobinæmia with hæmoglobinuria, but only a moderate increase of bile pigments. On the other hand, toluylendiamin, which in dogs causes but a moderate blood-destruction without hæmoglobinuria, causes a large increase of bile pigments. Thus it appears that the liver can be specially stimulated, and that the amount of bile pigment formed depends not only on the amount of free hæmoglobin available, but also on the activity of the liver-cell. Under certain circumstances this latter element may be so affected that hæmoglobin passes unchanged through it into the bile. This condition of "hæmoglobincholia" is usually the result of the action of certain severe poisons. Thus, according to Filehne (1889), after poisoning with phenylhydrazin, toluylendiamin, aniline derivatives, pyrogallic acid, chlorate of potash, and glycerine, all agents intensely hæmolytic in their action, hæmoglobin is constantly found in the bile. The same results, after poisoning with aniline and toluidin, have been found by Wertheimer and Meyer (1890). I produced such a "hæmoglobincholia" in one instance by ligaturing the hepatic artery and then injecting distilled water. All these observations apply to rabbits. In dogs, on the other hand, Filehne could never find any free hæmoglobin in the bile.

This passage of hæmoglobin unchanged through the liver-cell into the bile must be regarded, then, as betokening a grave disturbance of liver function. It is probably an extremely rare process in disease, and is probably confined to the last stages of such severe toxic conditions as acute yellow atrophy and the severest forms of malignant jaundice. But, apart from these extreme effects, this occurrence, rare though it be, is of interest as denoting that the activity of the liver in breaking up hæmoglobin can be directly influenced by drugs.

In what way the destruction is effected within the liver-cell we have no definite knowledge. As I have pointed out, an increased formation of bile pigments may occur while the formation of bile acids is diminished, indicating that the two processes, of hæmoglobin-destruction and breaking up of proteid material, respectively underlying these are to a certain extent independent of each other. Nevertheless certain interesting observations, to which I must now draw attention, no less clearly indicate that the activity of the liver-cell in breaking up hæmoglobin depends upon its general nutritive activity.

Schmidt and his pupils have studied the action of liver-cells on hæmoglobin outside the body, and they find that the destruction of hæmoglobin (and formation of bile acids) is much increased by the presence of glycogen, and still more of grape sugar; in the absence of these, indeed, the destruction of hæmoglobin ceases.

Lessened formation of bile pigments.—Again, among the conditions which appear to diminish the amount of bile pigments I have to note *fever*. This sequence was very noticeable in the case of biliary fistula recorded by Paton and Balfour. Irregular attacks of fever occurred from time to time, and during these the bile not only fell in quantity, as also in the amount of solids, but became obviously pale; on several occasions, indeed, quite colourless.

This diminished formation of bile pigments is of special interest in relation to the theory of jaundice by suppression. This theory took its origin when it was thought that the bile pigments existed preformed in the blood, and that the only function of the liver was to excrete them. If the liver ceased to act, the pigments accumulated in the blood, and jaundice ensued. It is now certain that the bile pigments are formed by the liver, not within the blood. But the theory of a jaundice by suppression is still held by many; and the form it now takes is that any temporary inaction of the liver in forming bile pigments is bound to throw pigments into the circulation which would otherwise have been excreted; whereby jaundice is induced. Now I have shown one possible effect of such inaction, namely, that hæmoglobin passes through the liver-cell unchanged. But such an event is only producible experimentally by the action of severe poisons, and even then with difficulty; in disease it is probably of the rarest occurrence. The other possible effect is that illustrated by the action of fever, when less bile pigment is formed. There is no evidence, however, that such a diminished formation of necessity produces jaundice. On the contrary, in the case of the great majority of poisons that act most severely on the liver-cells, and are most likely to cause suppression of function, there is direct evidence that they stimulate the liver to an increased formation of bile pigment. The jaundice they give rise to is not a jaundice of suppression, but one of increased activity with increased viscidity of bile consequent on the action of the poison on the intrahepatic bile-ducts (toxæmic catarrh).

Qualitative variations in the bile pigments.—The changes in the bile pigments in disease are not restricted to mere variations in quantity. They extend also to the quality of those formed.

In health, as we have seen, the chief pigments are bilirubin and biliverdin. Within the intestine these are reduced by the action of the micro-organisms present to hydrobilirubin (stercobilin)—the colouring matter of the fæces.

Relation of bile and urinary pigments.—Within the urine the chief pigments are:—

i. *Urochrome*, first described by Dr. Thudichum in 1864, and recently, with the aid of much better methods, carefully studied and redescribed by Dr. A. E. Garrod (1896).

ii. *Urobilin*, the relation of which to bile pigment, long a matter of discussion, may now be regarded as definitely settled. It has been shown to be producible directly from bile pigment by the action of the micro-organisms of the intestine (Müller); and more recently, in a very careful research, Garrod and Hopkins have shown that the pigment of the fæces, variously named hydrobilirubin or stercobilin, is only an impure form of urobilin.

iii. *Urohæmatoporphyrin* was first described by MacMunn, and has since been shown to be a constant constituent of normal urine (A. E. Garrod), and to undergo variations in disease. It is the representative in the urine of hæmatoporphyrin, a pigment formed from hæmoglobin.

The last two pigments are undoubtedly derived from hæmoglobin. The origin of urochrome, long obscure, seems also to have been placed beyond doubt by recent observations (1897). This pigment and urobilin are convertible into one another by the action of suitable agents.

Increase of the pigment of the urine is a common feature of liver disorder. Not only those above named become increased, but others also, of doubtful nature, make their appearance. The chief of these is the reddish pigment (*uroerythrine*) which so frequently colours deposits of urates.

The questions that now present themselves are:—Does the increase of such pigments indicate disorder of hepatic function especially; or, on the other hand, indicate merely disorder of intestinal functions? Or as it may otherwise be put:—To what extent are these pigments derived from the bile pigments within the intestine, and thus only indirectly from the liver? Or, are they the direct products of hepatic metabolism, formed by the liver just as bile pigments are?

With regard to urobilin,—the chief representative of these urinary pigments, and the one which has been most fully studied in disease,—an increase is found in the urine in a number of conditions, such as fever, absorption of blood, pernicious anæmia, febrile forms of jaundice, and the action of certain drugs, such as trional. These conditions are chiefly such as are marked by some increased destruction of blood. The increase of urobilin may denote merely an increase of bile pigments with an increased formation of urobilin from these within the intestine, and not necessarily any disturbance of hepatic function. A notable increase of bile pigment takes place during absorption of extravasated blood, as shown by Stadelmann; and according to my observations in pernicious anæmia no feature is more constant or more striking than the extraordinary colouring power of the bile, denoting great richness in pigments. And in no two conditions is urobilinuria so marked as in these.

There are other facts, however, which denote that the intestine is not the only seat of origin of urobilin; it is also formed elsewhere in the body. Thus in cases of obstructive jaundice where no bile enters the intestine urobilin is still found in the urine. In the case of biliary fistula described by Copeman and Winston no bile entered the intestine, nor was any bile pigment to be found in the urine. All the bile escaped through the fistula. Nevertheless the urine remained of normal colour, and its colouring matters must therefore have been formed elsewhere than in the intestine. Under these circumstances it is assumed that the pigment has been formed within the liver itself, as a direct product of hepatic activity. And it is from this point of view that so much interest is attached by some observers to increase of urobilin (and other pigments) in the urine in relation to hepatic disorder; for an abnormal increase of urobilin may thus denote not merely an increase of bile pigments, but also an abnormal activity of the liver-cell, and may be an index of hepatic disorder. Thus urobilin has been regarded as essentially the pigment of a diseased liver

(Hayem). Its formation by the liver may, I think, be thus conceived. Formed in small amount in health, as a by-product in the course of the formation of bile pigment by the liver-cell, in disease it may be formed in disproportionately large amount, not from the bile pigments, but, so to speak, at the expense of the bile pigments. An increase of urobilin in the urine may denote not merely an increased hæmolysis with an increased formation of bile pigment—this it necessarily does—but it may denote, further, some hepatic inefficiency in dealing with the hæmoglobin or pigments derived from this hæmolysis. I would point out a third alternative:—The conditions in which it is chiefly met with — toxic forms of jaundice, pernicious anæmia, and the like—are chiefly those denoting marked disorder of the blood, and the fault may possibly be not so much increase of bile pigments (intestinal origin) or hepatic inefficiency (hepatic origin) as some abnormal character of the hæmoglobin and other pigments set free within the portal area and conveyed to the liver in the portal blood. I consider it to be probable that some part of the urobilin and chromogens of the urine are normally formed within the portal area, notably within the spleen, where, according to my observations, hæmolysis is most active; and their increase in disease may denote abnormal blood changes antecedent to any subsequent hepatic inefficiency.

In deciding to which of these various possible causes urobilinuria is due in any particular case, we must be guided, I think, by the general characters of the symptoms rather than by any particular view as to the source of urobilin. Thus, in absorption of extravasated blood, I regard the urobilinuria as not necessarily of the same significance as it has in severe forms of febrile (toxæmic) jaundice. In all cases it denotes increased hæmolysis. But subject to this, it may in some denote intestinal derangement—increased putrefactive changes, with increased formation of urobilin from the bile pigments within the intestine; in others it may denote abnormal hæmolysis with formation of abnormal pigments in the tissues (extravasated blood) or in the spleen; and lastly, in a third group it may possibly denote hepatic inefficiency in dealing with the hæmoglobin supplied to it. The data we possess, then, by no means justify the view that urobilin is essentially the pigment of hepatic disorder.

Bilirubin calculi.—Before passing from this subject of the variations in the character of the bile pigments presented in disease, and their possible significance in relation to disorder of the liver, I must refer to one other modification of a qualitative character, which may not only denote but actually be the immediate occasion of severe disorder of the liver; I refer to that change which leads to the precipitation of bilirubin in insoluble form within the intrahepatic bile-ducts or within the gall-bladder, and to the formation of bilirubin calculi.

Bilirubin itself is never precipitated; but under certain conditions it forms a combination with calcium, and is then precipitated as an insoluble compound. In this form it is the nucleus of a considerable proportion of the ordinary gall-stones; in a smaller proportion it is itself the calculus, nd may constitute the gritty particles—the so-called biliary sand—found ithin the intrahepatic ducts, or the small calculi found either in these ucts or in the gall-bladder.

Two forms of these calculi are met with; in the one the bilirubin-alcium is mixed with cholesterin, as much as 25 per cent of the latter eing present; the remainder being made up of bilirubin-calcium, usually ith small quantities of copper and traces of iron. The calculi of his kind are usually of large size, as large as a cherry or larger; and e singly, or at most in groups of three or four, in the larger bile-ducts r gall-bladder. In the other form this insoluble compound of bilirubin orms the whole calculus. These stones are of small size—from that of grain of sand to that of a pea—and form solid brownish black concreions with rough, irregular surfaces; sometimes of wax-like consistence, ometimes firm, hard and brittle. They consist almost entirely of the alcium compound of bilirubin or biliverdin, without any cholesterin, or t most with mere traces of it.

Besides these forms of calculi, in which it forms the chief constituent, ilirubin-calcium is a common constituent of most gall-stones, either ntermixed with the cholesterin or sometimes forming the central nucleus.

A special interest attaches to these calculi of bilirubin-calcium; inasmuch as, unlike the ordinary mixed cholesterin calculi, the seat of the ormation of which is the gall-bladder, or very rarely the larger bile-ucts, small bilirubin-calcium calculi are frequently found in the intraepatic ducts. What determines their formation? Both bilirubin and alcium are normal constituents of the bile. Yet in whatever amount hey are present, or however highly the bile may be concentrated, they an never be made to combine to form this insoluble compound. Mere xcess of bilirubin appears insufficient of itself to bring this about in ormal bile. Addition of lime water, however, leads eventually to a preipitation of bilirubin-calcium. But certain substances in the bile appear apable of hindering this precipitation even when lime is present in bundance. The bile salts possess this power. Naunyn finds that in the resence of bile salts the calcium combines at first with the bile acid; and t is not until a large excess of lime is added that precipitation takes place. t is not likely that the precipitation of this compound is solely deendent upon an increase of lime in the bile. It is suggested that excess f lime in drinking-water may give rise to calculi by favouring the preipitation of bilirubin-calcium; there is no evidence, however, that the mount of lime in the bile is affected by the administration of lime in he food (Naunyn). Its source in all probability is the mucous membrane f the bile passages, as pointed out by Frerichs. More important than ny mere increase of lime or amount of bile pigment in determining the recipitation of bilirubin-calcium is the presence or absence of albumin in he bile. Thus egg albumin brings about a precipitation of bilirubin-alcium from bile, and from a solution of bile salt containing bilirubin. t is highly probable, then, as Naunyn says, that albumin is the chief actor in determining the precipitation of these biliary concretions

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These small intrahepatic calculi of bilirubin-calcium seem to play an important part in producing cholelithiasis. They are carried into the gall-bladder, where they act on its mucous membrane as foreign bodies, and favour the catarrhal condition which leads to the formation of cholesterin. In the centre of gall-stones a small nucleus of this compound is frequently to be found.

Conclusion.—The precipitation of bilirubin in insoluble form, with the production of biliary concretions of bilirubin-calcium, is thus to be regarded as evidence of disorder of the bile passages, not of the liver-cell itself.

Excretion of bile salts.—The salts of the bile are the soda salts of the two bile acids, glycocholic and taurocholic acid. The bile acids are combinations of a common acid—cholalic acid—with glycocine and taurine respectively; products of the decomposition of albuminous material within the liver. The formation of bile acids is thus a special index of the amount of albuminous metabolism within the liver-cell. How closely it is related to other functions of the liver-cell is indicated by the interesting studies made by Schmidt and his pupils, to which reference has already been made. They find that even outside the body the liver-cell can form bile acids from albumin, but that it cannot do so unless glycogen, or, what is even better, grape sugar, be present.

The fate of the bile acids within the intestine is interesting. A small proportion only can be accounted for in the fæces. A large proportion, as much as seven-eighths according to Bidder and Schmidt, is again absorbed and again excreted in the bile. It is this remarkable behaviour of the bile salts that has led to the view, originally propounded by Schiff, that there exists within the portal area "a circulation of bile." The bile obtained from a fistula is much poorer in solids than normal bile, and the difference is almost entirely due to want of bile salts. No substance or drug has so powerful a stimulant action on the liver-cell as its own bile salts.

We have little information as to the variations in their excretion met with in disease. Clinically our chief interest is directed to the bile salts in connection, first, with their solvent action on cholesterin, the chief constituent of gall-stones; and, secondly, with their appearance in the urine in cases of jaundice. Cholesterin is held in solution in the bile mainly by the presence of the bile salts; it is insoluble in water or aqueous saline solutions, but easily soluble in solutions of the bile salts; solutions containing ¼ to 2½ per cent of bile salts can dissolve about a tenth part of their own mass of cholesterin (Naunyn). One of the oldest views of the origin of gall-stones is, that owing to decomposition of the bile acids within the gall-bladder, the cholesterin is no longer held in solution and becomes precipitated (Frerichs). There is no conclusive evidence, however, that calculi ever arise in this way. The evidence presently to be considered goes rather to show that gall-stones arise from increased secretion of cholesterin from the walls of the gall-bladder, not *from simple precipitation of the cholesterin held in solution.*

Much importance was formerly attached to the presence of bile acids in the urine in certain cases of jaundice, and to their absence in others, as an important gauge of the degree of activity of the liver. Since the bile acids are admittedly formed by the liver, and by the liver alone, their absence from the urine, in any case of jaundice, was held to be due to inactivity of the liver. Hence the view of a hæmatogenous as distinct from a hepatogenous jaundice. This matter will be considered fully elsewhere (art. "Jaundice"). Here it can only be said that the studies of Stadelmann have thrown an entirely fresh light on this subject. So far from the formation of bile pigments and of bile acids by the liver-cell necessarily going hand in hand, as hitherto assumed, these studies show that a large increase of bile pigments in the bile is frequently attended with a no less marked diminution in bile acids. This peculiar result is especially characteristic of the action of certain poisons which possess powerful icterogenetic properties (toluylendiamin, phosphorus). The jaundice caused by such agents is always marked by a greatly diminished formation of bile acids; and hence at the very time the urine is loaded with bile pigment there may be little or no trace of bile acids.

Pettenkoffer's reaction.—The test for the detection of bile acids in the urine is the well-known one which goes by the above name. A small quantity of the urine is placed in a porcelain capsule, and to it two or three drops of a solution (10 per cent) of cane sugar are added. Then strong sulphuric acid is added drop by drop, when the fluid first becomes opalescent, then clear, and successively assumes a pale cherry red, a dark red, and finally a purple-violet tint. The reaction depends, as it has since been shown, on the production of furfurol by the action of the acid on the sugar. Hence a modification of the test has been suggested, a solution of furfurol in water of 1 per mille being employed instead of sugar. To 1 c.c. of an alcoholic solution of the urine a single drop of this furfurol solution is added; then 1 c.c. of strong sulphuric acid. The method gives a perceptible reaction with quantities so small as even $\frac{1}{20}$th to $\frac{1}{30}$th of a milligramme. For clinical purposes the test is of little value, as the reaction is often given by other organic substances present in the urine. According to Prof. Halliburton, with whom I entirely agree, it is never possible to detect bile salts in the urine by the direct means of this test. They must always be separated by evaporating the urine to dryness, extracting with alcohol, and then precipitating the bile salts by adding 12 to 20 times its bulk of ether. The precipitate is then dissolved in water, and decolorised with charcoal before applying the test. Even then I have failed to get any definite reaction in cases of undoubted simple obstructive jaundice, where there was every reason to expect bile salts to be present; and I have got it where no bile was present.

Many substances present in the urine—such as albumin, fatty acids, and phenol compounds—give a reaction with Pettenkoffer's test, so closely resembling that of bile acids "that were it not for the method of spectroscopic observation we should be unable to pronounce an opinion *concerning the identity or non-identity of the colouring matters which are produced in each case" (Gamgee). Applied in the way usually* recommended for clinical purposes, the test is then, in my experience and judgment, quite useless. Further, the information it yields, even when accurately obtained, is hardly commensurate with the labour involved in acquiring it, now that it has been shown that the formation of bile acids by the liver varies so greatly, and that their presence or absence from the urine has not the significance formerly attached to them.

Excretion of cholesterin.—Cholesterin is a constant constituent of the bile; but, unlike the constituents just considered—the bile pigment and the bile acids—it is by no means peculiar to the bile. It is a substance very widely distributed in the animal body; it is especially abundant in nervous tissue, and is found also in the corpuscles and plasma of blood, in milk, sweat, in serous exudations, pus, and in the secretions of mucous membrane generally. It is held in solution in the bile by the bile salts and by the traces of fats and soaps present.

Cholelithiasis.—The chief interest attaching to it is that it forms the most abundant constituent of gall-stones. The conditions determining its amount and its solubility within the bile are thus of special interest. With regard to its source there is still difference of opinion. Its widespread distribution within the body would suggest that it is excreted by the liver. In cases of jaundice with complete obstruction it is said to accumulate in the blood (Frerichs), but this statement lacks confirmation. A more recent view is that it is not merely excreted from the blood, but that it is formed by the mucous lining of the gall-bladder and the larger bile-ducts (Naunyn), and that it is really a product of degeneration of the epithelium of their coats. According to the experiments of Naunyn, whose studies are the most exhaustive yet made, cholesterin is not simply excreted by the liver, for he found no noteworthy increase in the bile after administration of large quantities of cholesterin, both by the mouth and subcutaneously; he concludes, indeed, that no separation whatever of cholesterin from the blood takes place through the bile. He finds, moreover, that the amount of cholesterin is not dependent upon diet. He also investigated the excretion of cholesterin in various diseases, but failed to find any notable increase of the substance, unless gall-stones were also present. He concludes, then, that the cholesterin of the bile is neither a product of general metabolism nor a specific secretion product of the liver.

On the other hand, the secretion of mucous membranes constantly contains cholesterin, sometimes in no less quantity than the bile itself. In bile the proportion varies from 0·5 to 3·5 per 1000. In sputum of catarrhal bronchitis Naunyn found it to the amount of 0·9 in 1000, and in sputum of putrid bronchitis he found it to the amount of 1·5 per 1000. In pus it has been found in even higher amounts. In all these cases there has been actual inflammation and an abnormally large amount of degeneration of cells and epithelium; and Naunyn thinks it probable that a considerable shedding of epithelium from the biliary passages, *induced by the deleterious action of the bile itself (as a protoplasmic poison), constantly goes on.*

Whatever view we may take of the source of the cholesterin of the bile in health, whether hepatic, as Frerichs and Gamgee maintain, or biliary, as Naunyn suggests, there can be little doubt, I think, that the latter is its source in disease. An increased formation of cholesterin in connection with subacute inflammatory and catarrhal conditions of the lining membrane of the bile passages, especially of the gall-bladder, is the chief factor underlying the formation of gall-stones in disease. The cholesterin which goes to form gall-stones has never been in solution in the bile. It is formed as viscous material within the degenerated epithelium thrown off from the gall-bladder; and it collects, as such, either around amorphous particles made up of degenerated epithelium, or around small solid concretions of bilirubin-calcium. Once formed, the calculus grows by further accretion either of cholesterin or bilirubin-calcium, or both. The cholesterin, according to Naunyn, may accumulate in two further ways; it may come either from degeneration of the epithelium lying around it, as in the cases in which a stone lies in a pocket embracing it so closely that no bile may have entered for some time; or, on the other hand, when the stone is bathed in bile, it may grow by crystallisation of the cholesterin in the bile. But this mode of increase is rare. In the great majority of calculi the superficial layer is not crystalline, but at first is amorphous; it is at a subsequent date that this amorphous cholesterin undergoes crystallisation.

What is it that determines this increased formation of cholesterin?

The facts with regard to the general etiology of gall-stones are well known. Gall-stones are uncommon in young people under 30 years, and most common in old people over 60. They are much commoner in women than men—among males in 4·4 per cent of bodies examined, among women in 20·6 per cent. Among women they are much more frequent in those who have borne children. Thus it appears that the formation of gall-stones is facilitated by anything which interferes with or retards the flow of bile; as, for example, by the habit of lacing in women, which diminishes the movements of the diaphragm; by pregnancy, which acts in the same way; by the less active habits of advancing life, and the atrophy of muscle which attends it. According to Charcot, the unstriped muscular fibres of the walls of the bile-ducts undergo extensive atrophy in old people. Stagnation of bile is an etiological factor about which there is no dispute.

How, then, does stagnation of bile lead to the formation of biliary calculi? We have seen that such formation is the result of morbid processes in the lining membrane of the gall-bladder; Frerichs taught that in stagnating bile the bile salts were apt to undergo decomposition, the reaction of the bile to become acid, and the cholesterin, previously held in solution by the bile salts, to be precipitated. The recent observations of Naunyn throw another light on the subject. According to Naunyn, the catarrh responsible for the increase of cholesterin is set up by presence of micro-organisms. Normal bile is sterile; Gilbert and Girode found it so in 6 out of 8 cases, even 24 hours after death; Naunyn found it so in 4 cases, and I found it so in 2 out of 3 cases. But when it stagnates, organisms may be found in it. The organism most commonly present under such circumstances is the *Bacillus coli communis;* and this organism Naunyn regards as the commonest cause of the disease of the mucous membrane which leads to the formation of stone. The sequence of events he considers to be stagnation of bile, favouring invasion of this organism; then some degree of cholangitis and cholecystitis, which this organism can undoubtedly cause, and, as the result of this inflammation, formation of gall-stones and cholelithiasis.

The importance of stagnation of bile is evident from certain experiments made by Naunyn. After ligature of the common duct, the injection of this organism caused acute inflammation of the bile passages and death of the animal. On the other hand, its injection into the healthy ducts without previous ligature produced no symptoms whatever.

The invasion of the bile passages takes place from the intestine. Invasion from the blood plays no part in the etiology of cholelithiasis. Prof. Sherrington found that at a time when the blood was teeming with organisms there might not be the slightest penetration of them into the bile. When organisms do appear in the bile, as undoubtedly they do, this occurs later, when some damage has occurred to the walls of the capillaries.

An important point remains to be noted. For the formation of gall-stones in the number that we so often meet them, it is by no means necessary to assume a continuous infection with organisms. On the contrary, what probably happens is that a transitory invasion suffices to set up a certain degree of catarrh sufficient to lead to the formation of a few gall-stones. Afterwards the gall-stones themselves, even in the absence of organisms, suffice as the irritant: they irritate the mucous membrane mechanically, and lead to an increased formation of cholesterin, and by causing obstruction favour subsequent reinfection.

Conclusion.—Thus it appears that the large group of morbid conditions comprised under the term cholelithiasis are due primarily to disorder of the bile passages, not to functional disorder of the liver.

Excretion of drugs and poisons.—The excretory functions of the liver are not confined to the more or less specific constituents just considered, but extend also to a class of other substances, medicinal and otherwise, which may be present in the blood. Thus it has been shown that a number of drugs, when given by mouth or injected subcutaneously, are to be found in the bile; for example, zinc, ferrocyanide of potassium, iodide of potassium, cane and grape sugar, sulphate of copper, oil of turpentine, bromide of potassium, iron, lead, nickel, arsenic, silver, bismuth, antimony, carbolic acid, salicylate of soda, toluylendiamin, chlorate of potash. In some cases this excretion takes place very quickly.

Thus Peiper found salicylate of soda in the course of half an hour after its administration by the bowel; iodide of potassium after some six to eight hours. In the case of toluylendiamin, a drug notable for its power of inducing jaundice in dogs, I was able to detect it in the bile within half an hour of its intravenous injection; and in three to four hours it was present in quite an appreciable, albeit very small quantity. In respect of such substances the liver is, however, no mere filter. While excreting some of them, others it appears to arrest or destroy. Thus atropine, muscarin, strychnine, kairin, antipyrin, quinine are not to be found in the bile after their administration.

This power of arresting poisons is one of the most important functions discharged by the liver, as it prevents the escape into the general blood current of crude products of digestion, many of which possess poisonous properties. Thus Roger (1893), experimenting on guinea-pigs, found that a watery extract of liver was some sixteen times more poisonous than that of muscle, and about five times more poisonous than that of kidney.

There are two sets of observations with regard to the action of the liver upon strychnine: Jacques found that a dose of 0·74 milligramme per kilo injected into the portal vein of a dog caused scarcely any noticeable effect, whereas less than the half of this dose (0·36), injected directly into a peripheral vein, killed the animal in three minutes. Roger made a number of comparative experiments on healthy frogs, and on frogs deprived of the liver. (The latter animals live four to five days.) While a healthy frog survived the injection of 0·03 milligramme of strychnine for 40 hours, a smaller dose (0·02) killed the liverless frog in 17 hours. The results were still more striking if smaller doses were injected more gradually (over an hour). Thus a healthy frog received 0·016 milligramme subcutaneously without any ill effect; while a smaller dose (0·012) killed the liverless one with violent convulsions.

As regards atropine, some interesting experiments of Kotliar (1893) made on dogs seem to point to a similar conclusion, namely, that the liver has a protecting power against its action. If the poison were made to pass through the liver, the animal was more resistant than in the case of direct injection into the general blood current.

As suggested by Dr. Lauder Brunton, some interference with this function of the liver in regard to alkaloidal and other deleterious products reaching it from the intestine is probably accountable for certain of the more common symptoms usually ascribed to disorder of the liver, such as a bitter taste in the mouth, giddiness, cloudiness of intellect, drowsiness, irritability, depression. Products which the healthy liver ordinarily destroys may escape into the general blood.

This function is indeed bound up with the general metabolic activity of the liver-cell. Thus leucin and tyrosin—secondary products formed in pancreatic digestion—are arrested and transformed within the liver-cell. In cases where the liver undergoes excessive degeneration, as in acute yellow atrophy or phosphorus poisoning, these products pass through unchanged and appear in the urine. Along with them doubtless pass a series of other products normally arrested by the liver.

Another fertile source of disturbance is the excretion of such products into the bile. In relation to the pathology of jaundice and disorder of the bile passages generally, this excretory function of the liver is, I consider, all-important. The power possessed by certain drugs and organic poisons of causing jaundice is, according to my observations, connected with their irritant action on the lining of the bile passages in the course of their excretion by way of the bile. Such poisons usually cause more or less marked changes in the blood. But, as I have shown, their power of inducing jaundice is proportioned, not to the action on the blood (phosphorus, for instance, has no hæmolytic action at all), not to the amount of hæmoglobin set free, not to the amount of bile pigments formed, but solely to the degree of viscidity of the bile induced.

It is in this relation that the observations on the excretion of toluylendiamin through the bile are of most interest. This drug is the most notable of all icterogenetic poisons; and my observations with regard to it (1895) show that the increase of viscidity of the bile, which is the immediate cause of the obstructive jaundice, is the direct result of the irritant action of products in the bile. So irritant, indeed, is its action that, with large doses, an intense inflammation of the duodenum can be set up, definitely beginning at the orifice of the bile-duct where the poison (injected subcutaneously) reaches the duodenum. When the action of the drug is at its height the whole of the intrahepatic ducts are found filled with thick viscid bile. Lower down colourless mucus fills the common duct, and may be seen exuding slowly through the opening of the bile papilla into the duodenum. The duodenum is also filled with similar viscid mucus free from bile; its mucous membrane is acutely inflamed, red, studded with punctiform hæmorrhages, and swollen to three times its normal thickness. The whole of the bile passages, in short, are in a condition of acute catarrh, set up presumably by products contained in the bile. For be it noted the catarrh is of intrahepatic, not of duodenal origin. It extends from the smaller ducts down to the duodenum. Affection of the duodenum is indeed by no means necessary. The catarrh and the accompanying jaundice are producible even when the common bile-duct has been ligatured and a biliary fistula established.

The production of catarrh in this way, by excretion of products in the bile, I consider to be, as I have already pointed out, a most important fact in relation not merely to severe forms of jaundice produced by poisons, but to the pathology of liver disorders generally.

The normal products of digestion, carried to the liver and excreted in the bile, are non-irritant. If at any time, as the result of impaired digestion or other such cause, abnormal products are formed in the intestine and absorbed into the blood, the duty falls upon the liver to arrest them, either by modifying them or by excreting them. This function it discharges successfully, and in the great majority of cases probably with little or no disturbance to itself; for it is with crude products that it is accustomed to deal. Did it pour its secretion directly into the intestine, no disturbance would arise,—no further opportunity would be given for any of the abnormal products to produce ill effects. As it happens, however, the bile, with any injurious products it may contain, has to pass at a low pressure along the system of bile passages lined with epithelium, the larger of them having a mucous lining supplied with mucous glands. If, then, such products have any irritant qualities whatever, the effect is to increase the amount of secretion thrown off from the epithelium of the bile passages; and in proportion to the increase of mucus there is a tendency for the flow of bile to be retarded.

Fortunately only certain organic poisons, and these not common ones, possess irritant qualities to any notable degree. Their action is similar to that of toluylendiamin, in that they cause such an increase of viscid mucus that the flow of bile is temporarily arrested, and jaundice results. The obstruction then is chiefly intrahepatic. Of this nature, I consider, the various more or less specific forms of jaundice are—"epidemic" (catarrhal), probably also ordinary "catarrhal" jaundice; "malignant jaundice," "febrile jaundice," "infectious jaundice (Weil's disease)," "acute yellow atrophy of liver," also the jaundice of yellow fever, relapsing fever, malarial fevers, pyæmia, and other febrile conditions.

But probably many products of abnormal digestion possess some irritant quality; falling far short indeed of that above described, but yet capable of producing a certain amount of disturbance. The excretion of these may occasion a certain retardation in the flow of bile, and thus lead to some absorption of bile constituents. This is one of the conditions underlying the ailments variously known as "biliousness," "torpor of the liver," and cause the icteric tinge of conjunctivæ characteristic of these ailments.

It is easy to understand how the liver-cell, which originally had escaped injury, may suffer in its functions secondarily to this condition of bile and bile passages; how, in short, many of the classical symptoms of "lithæmia" may arise—not merely a sluggish flow of bile, but also an altered metabolism, evidenced by increase of urates and uric acid in the urine characteristic of the condition; and how by the continuance of the disturbing factors—faulty products conveyed to the liver on the one hand, retarded excretion along the bile passages on the other—we may have biliousness established as a more or less chronic habit of body.

The primary fault lies not with the liver, but with the organ responsible for the products conveyed to it in the portal blood. Under these circumstances, to speak of "lithæmia" as a substantive condition due primarily to disorder of liver function, as Murchison does, is hardly justified. The only fault in the liver may be that it merely excretes certain of the abnormal products into the bile, and fails to destroy or modify them on the way. But to excrete can be hardly deemed a primary error of function on the part of an excreting gland.

While, therefore, fully recognising the important part played by disturbance of liver function in disease, it is in my view no less important to recognise the precise relation in which such functional disturbance stands to disease elsewhere. In most cases it is not the primary disorder, but is itself the result of functional disturbance elsewhere; either in the organs responsible for the products supplied to it, or, as in the cases just considered, in the bile passages.

So far I have considered this condition of intrahepatic (toxæmic) catarrh solely in relation to jaundice and biliousness, and to the condition termed lithæmia. I have now to point out that in relation to cholelithiasis and the formation of gall-stones it may also play an important part. We have seen that in many cases the nucleus around which the deposit of cholesterin takes place is formed of the insoluble body bilirubin-calcium, that in a number of cases the calculi may consist entirely of this material, and that, unlike the ordinary calculi consisting of cholesterin, which are formed exclusively in the gall-bladder, small calculi of bilirubin-calcium are not infrequently found in the intrahepatic ducts, either as "bile sand" or as definite calculi. We saw, moreover, that what determined more than anything else the precipitation of bilirubin in this insoluble form was the presence of albuminous matter. It is thus extremely probable that long-standing conditions of intrahepatic catarrh, by leading to shedding of epithelium, may be the chief etiological factor in the formation of this bile sand. And thus indirectly it may be a potent factor in the production of larger gall-stones; inasmuch as we saw reason to believe that, apart altogether from microbic infection of the bile passages, these small calculi of bilirubin-calcium might, in certain cases, by the mechanical irritation they set up within the gall-bladder, lead to the formation of cholesterin.

Conclusion.—Disturbances of the excretory functions of the liver play the chief rôle in the production of functional disorders of the liver.

Digestive functions.—The functions of the bile in digestion, long regarded as of the first importance, have now been shown to lie within comparatively narrow limits. On starches and proteids, the two chief food constituents, it exerts practically no action whatever. Its action is restricted to fats, which it emulsifies, thereby facilitating their absorption.

When bile is cut off from the intestine, the fæces contain a large excess of fat; instead of containing only about 1 per cent of the fat administered, the amount thus lost may be as much as 66 per cent. It is the presence of this fat which gives the peculiar clay colour to the fæces in cases of obstructive jaundice; it may constitute as much as 11 to 13 per cent of the weight of the fæces. It may be in part responsible for the peculiar sickening fœtor which fæces free from bile usually have; but Gamgee, on the other hand, has observed the complete absence of fœtor, in spite of large quantities of unabsorbed fat, in cases of fatty stool due to disease of the pancreas without pressure on the common bile-duct. It is certain, however, that if dogs with biliary fistula be fed on carbohydrates instead of fat, the fœtor in great part disappears.

It is this peculiar fœtor of the fæces in the absence of bile that has led to the view that the bile has powerful antiseptic properties. It certainly has no direct antiseptic action, for micro-organisms of various kinds have been shown to grow freely in media containing bile (Copeman and Winston, Sherrington). On the other hand, it is found by other observers, as pointed out by Gamgee, that free bile acids have powerful antiseptic properties. It is probable that as soon as the bile comes into contact with the intestinal contents, the bile salts are decomposed, and bile acids set free; and it has been suggested (Gamgee) that the presence of these acids may modify in some way the putrefactive changes which albuminous substances undergo in the intestine. Whether this be so or not, it is certain that their place may be taken by other agents. For in the case of biliary fistula recorded by Mayo Robson, where for fifteen months all bile was discharged externally, the odour of the fæces did not differ from that of a healthy motion, and the bowels were quite regular throughout without the use of aperients. That the presence of bile is not essential to good nutrition, is further evidenced by the case of biliary fistula recorded by Paton. The woman returned after a year's interval in a state of robust health, having put on a stone in weight notwithstanding the complete absence of bile from the intestine.

REFERENCES

1. BUNGE. *Physiologische und pathologische Chemie* Leipzig, 1887.—2. COPEMAN and WINSTON. "Observations on Human Bile obtained from a case of Biliary Fistula," *Jour. of Physiol.* vol. x. p. 213, 1889.—3. EIFFELMANN. *D. Archiv f. klin. Med.* xxiv. p. 228.—4. FILEHNE. *Virchow's Archiv*, cxvii pp. 115-117, 1889.—5 GAMGEE. *Physiological Chemistry of the Animal Body*, vol ii. Macmillan & Co. 1893 (The reader is referred to this for an account of the subject of the Bile which is admirable in all respects.)—6. GERALD F. YEO and E. F HERROUN. "A note on the composition of Human Bile obtained from a Fistula," *Journal of Physiol.* vol. x. p. 116 —7. GLASS. *Archiv f. exp. Path.* xxx. pp. 241-274, 1892.—8. HALLIBURTON. *Text-Book of Chemical Physiology and Pathology*, 1891.—9. KOTLIAR. *Archives des sciences biologiques*, vol. ii. pp. 586-631, 1893—10. LEWASCHEW. *D. Archiv f. klin. Med* xxxv. 1884.—11. MAYO ROBSON. "Observations on the Secretion of Bile in a case of Biliary Fistula," *Proc. Royal Soc.* vol. xlvii. p. 499, 1890.—12. NAUNYN. *A Treatise on Cholelithiasis*, Syden. Soc. Trans., by A. E. Garrod, 1896.—13. NISSEN *Jahres. u. thier. Chemie*, xx. 1890.—14. NOEL PATON and BALFOUR. "On the Composition, Flow, and Physiological Action of the Bile in Man," *Labor. Reports, Edin Royal College of Physicians*, p. 191, 1891.—15. NOEL PATON. *Ibid.* vol. iv. 1892.—16. PAIJKULL and HAMMARSTEN. "Ueber die Schleimsubstanz der Galle," *Zeitsch. f. physiol. Chemie*, xii. p. 196, 1887.—17. PISENTI. *Arch. f. exp. Path.* xxi. p. 219, 1886.—18. PREVOST and BINET. *Compt. rend.* cvi. p. 1690, 1888.—19. ROGER. *Archiv d. Physiol.* vol. xxiv. 1893.—20. ROSENBERG. *Pfluger's Archiv*, xlvi. 1889.—21. WERTHEIMER and MEYER. *Compt. rend.* cviii. pp. 357-359.

For other references see art "Jaundice."

CONGESTION OF THE LIVER

SYNONYM.—*Hyperæmia of the Liver.*

Definition.—*A pathological condition associated with a number of diseases, not itself constituting a disease, but conveniently considered separately on account of the size and importance of the organ; consisting in the* presence of a large excess of blood within the blood-vessels of the liver; clinically characterised by a varying degree of enlargement of the organ beyond physiological limits and by disturbances of liver function; caused by two distinct sets of conditions, one of chemical (gastro-intestinal) origin—"active congestion," the other of mechanical (cardiac) origin—"passive congestion"; resulting in recovery on removal of the cause.

Varieties. — The condition known as "congestion of the liver" cannot be regarded as a distinct disease. Under any circumstances the border-line between physiological and pathological hyperæmia of any organ is ill defined; and this must especially be the case in an organ subject, like the liver, to great physiological variations in the quantity of blood it contains. If therefore a pathological condition like congestion, common in varying degree to all organs alike, be dignified with the title of disease, it must be on some special ground, such as the size of the organ or the importance of its functions, and the consequent gravity of the effects connected with disturbance of them. Examples of such organs we have in the case of the brain and spinal cord.

It is only on this ground that congestion of the liver has any claim to be considered as a formal malady; for it is always associated with and depends upon diseased conditions elsewhere—notably, for instance, upon congestion of the gastro-intestinal tract. In the case of the gastro-intestinal tract the effects of congestion are widespread and ill defined; in the case of the liver they are concentrated, and thus arrest the attention alike of patient and medical observer. These effects in the liver occasion a distinct local distress, as well as more general symptoms referable to disturbance of the gastro-intestinal functions.

Again, the liver is particularly subject to congestions, partly on account of the character and the richness of its double blood-supply; partly on account of its situation at the outlet to the portal system on the one hand, and of its neighbourhood to the heart on the other. Thus it has to share in every congestive trouble arising throughout the extensive area from which the portal blood is drawn; while its proximity to the heart renders it one of the first organs to be affected by any obstruction to the flow of blood through the right side of the heart.

According as the increase of blood is brought about by *increased inflow* through the portal vein, or *obstructed outflow* through the hepatic veins, it is possible to distinguish *two varieties of congestion of the liver*, different alike in their causes, their clinical features, and their pathology. Hence the distinction between them is of practical importance. The congestion due to obstructed outflow is rightly called "*Passive*," as it is brought about by mechanical causes, and is attended with corresponding lesions—such as dilatation of capillaries, fatty degeneration, and atrophy of cells—the results of increased pressure. That connected with increased inflow, on the other hand, is in the first instance an exaggeration of the normal condition of the organ during the times of its activity; it is the result of chemical and nervous influences, such as operate in health during digestion; and the anatomical changes are also those of increased activity, and not of increased pressure. This form again is rightly called "*Active*." As an independent affection it is this latter form of congestion only that really needs consideration. Passive congestion of the liver is best described under the title of "the cardiac liver," usually given to it by French writers, and considered as one of the sequels of heart affections.

ACTIVE CONGESTION.—*Conditions influencing the quantity of blood in liver.* —Rightly to understand the causes of active congestion it is necessary to have in mind the chief conditions influencing the circulation within the liver in health. Of these the first and most important is *digestion*. An increased flow of blood through the liver with considerable increase in its size is an event of daily periodic occurrence during the process of digestion. The greater part of this inflow is the result of that general vascular dilatation throughout the gastro-intestinal area which attends the process of digestion, and the consequent greater inflow of blood into the portal system. To a much less extent the inflow is due to a corresponding dilatation of the hepatic artery; but the quantity of blood conveyed to the liver through this channel seems very small when compared with that carried to it by the portal vein. It is thus obvious that, to a much greater extent than is the case with other organs, the amount of blood within the liver is regulated by changes occurring outside it, namely, in the gastro-intestinal area. Whatever amount of blood is allowed to enter the portal system, as the result of the changes going on in that area, must necessarily pass through the liver, whether the liver be concerned in the activity of that area or not. As a matter of fact, however, the period of engorgement of the liver during digestion corresponds with the period of its greatest functional activity consequent on the supply of food products conveyed to it. The primary influence, therefore, regulating the amount of blood in the liver at any time, whether directly through the hepatic artery or indirectly through the stomach and intestine, is the presence or absence of food products in the portal blood. Or, as it may otherwise be expressed, *the degree of congestion of the liver in health is a question mainly of gastro-intestinal chemistry.*

This activity is doubtless conditioned by the nervous system, but of the nervous mechanism concerned we know but little. It is probably, in the main peripheral. But that there is also some central nervous control over the blood-supply of the liver appears in the well-known experiment of Claude Bernard in which, by puncture of the floor of the fourth ventricle, it is possible to induce intense (albeit only temporary) hyperæmia of the liver with glycosuria. Some vaso-inhibitory influence seems thus to be exerted on the organ directly from the brain; its course being down the cord as far as the third pair of dorsal nerves, thence into the sympathetic, and through the splanchnics to the liver. An opposing vaso-constrictor influence is attributed to the vagi. Whatever the nature of this central nervous control, there is little reason, except the experiment above noted, to suppose that it plays any prominent part in regulating the quantities of blood in the liver in health; and its part in disease is probably still less. The peripheral mechanism which I have indicated is resident in the vessels themselves.

Respiratory movements.—While, then, the chemistry of the gastro-intestinal area, acting through the nervous system, is the chief factor regulating the amount of blood within the liver, there is another factor the influence of which is not to be overlooked—namely, the influence of the respiratory movements.

The blood-pressure within the portal system is both feeble and variable, varying from 7 to 24 millimetres of mercury; that in the hepatic veins is still less, oscillating between a maximum of + 4 millimetres and a minimum of − 5 millimetres. When the pressure is at its lowest in the portal system, there is thus but little difference between it and that in the hepatic veins. The difference is sufficient, however, to enable the blood to pass from the portal into the hepatic veins, aided as the flow probably is by the rhythmical contractions of the trunk of the portal vein and intestinal peristalsis on the one side, and by the aspirating action of the right heart in diastole on the other. Of most importance, however, in this relation are the respiratory movements of the diaphragm. During inspiration the abdominal pressure rises, while the intra-thoracic pressure tends to fall; moreover, as the liver is directly pressed upon by the descending diaphragm, the flow of blood through the liver is greatly facilitated by both means. Both a suction and a forcing power are exerted on the flow of blood during inspiration, and this is the greater the more forced and deeper the inspirations.

Exercise, therefore, which calls forth such forced movements in greater degree, greatly facilitates the flow of blood; while sedentary habits tend to its retardation.

Etiology.—The causes of active congestion of the liver in disease consist in an exaggeration or undue persistence of the conditions which favour physiological hyperæmia: these may briefly be described as *gastro-intestinal* in origin, and *chemical* in nature; and thus they are sharply distinguishable from those of "passive congestion," which are cardiac in origin and mechanical in nature. Two main groups of causes may be distinguished — (i.) gastro-intestinal, (ii.) toxic. The former group comprises the great majority of cases met with in this country, where the hepatic congestion is traceable to morbid congestions of stomach and intestine arising from errors in food and drink; the latter includes the cases, common rather in tropical climates, in which the *congestion seems to be due to some toxic influence, as in malaria, dysentery, yellow fever, icterus gravis, Weil's disease, bilious typhoid.* It will be noted, even in these cases, that the entrance of the poison is chiefly by the gastro-intestinal tract.

(i.) *Gastro-intestinal influences.*—The most common causes of active congestion of the liver undoubtedly are gastric catarrh and associated intestinal congestions set up by undue indulgence in food and drink. It is most commonly found in persons who habitually eat and drink much, and take little exercise. Rich and highly seasoned foods which tend to produce or aggravate the conditions of catarrh and congestion of the mucous membranes are potent for evil.

Excess in malt liquors, wines, or spirits is undoubtedly also a very potent cause of congestion, and more common perhaps than excess in eating alone. That these agents exert a directly injurious action on the liver itself is proved by the occurrence of cirrhosis of liver. It is in the habitual toper that the best-marked attacks of congestion of the liver are to be met with in this country.

Over-indulgence in liquids of any kind, especially if taken with food, also favours the occurrence of the condition in persons of plethoric habit of body.

Not only excess, however, but irregularities in the times of taking food, insufficient mastication, and other causes of gastric catarrh, will produce congestion of the liver in persons liable to it, for certain patients appear to have a proclivity to hepatic congestion. Such patients are usually of stoutish build of body, of phlegmatic habit, and of sallow, muddy, so-called "bilious" complexion. There is a want of tone about them generally, which seems especially to affect their portal vascular system. Causes which in ordinary persons would set up a temporary indigestion at worst will in them produce well-marked congestion of the liver.

Most of the above causes operate strongly at or near the middle age, when a sedentary life is more usual.

Congestion of the liver is frequently a premonitory sign of an attack of gout; and the connection between these two conditions was insisted upon long ago, chiefly by English observers (Scudamore, Gairdner, Garrod).

The foregoing causes operate by producing and maintaining conditions of congestion and catarrh in the stomach and intestine. Among the rarer causes may be mentioned dilatation of the stomach, which, according to Bouchard, may set up active liver congestion. This association I have also had occasion to note.

(ii.) *Toxic conditions.*—In warm climates the various forms of aguish and miasmatic affections, such as malaria, dysentery, and intermittent fevers, are active causes of congestion of the liver. To the same group also belong the various forms of febrile jaundice, such as yellow fever, icterus gravis, Weil's disease, and bilious typhoid, in connection with which congestion of the liver is a regular occurrence.

*It is probable that in most if not in all these cases the influence on the liver is brought to bear through the intestines, as in dysentery, malaria, bilious typhoid; and that it differs from that operative in the foregoing group of cases in being of a poisonous nature. Well-marked swelling and congestion of the liver are, in my experience, a common accompaniment of the action of the drugs which produce jaundice, such as toluylendiamin.

It is in connection with this group of affections that the *influence of climate* in favouring congestion of the liver may most conveniently be considered. So much more common is the malady in hot climates than in cold that it has been attributed to great heat alone independently of infections. But the two kinds of agency cannot be dissociated, nor should we forget the changed habits of life in food, drink, and exercise. According to the two French observers, Kelsch and Kiener, nearly all cases of congestion of the liver occurring in warm climates can be traced back to malaria, dysentery, and similar influences. At the same time changes of temperature greatly dispose to attacks by intensifying the operation of those dietetic and other influences which in more temperate climates are less effective. Cold also seems to play a part. The vague condition called "liver-chill" is regarded by some authors as a form of active congestion of the liver.

Lastly, there remain one or two other conditions which have been regarded as causes of congestion of the liver.

The first of these is *suppressed menstruation*, in connection with which some degree of congestion is said not infrequently to occur; sometimes with jaundice. Four such cases of "menstrual jaundice" are described by Senator. This variety of congestion is usually met with either at the catamenial period or at the approach of the climacteric; and it has been supposed to arise directly from vaso-motor disturbance. Perhaps these cases ought to be regarded as belonging to the large ill-defined group in which the title "congestion of the liver" is used as a convenient and popular name for ill-understood disorders.

In diabetes mellitus, also, some degree of congestion occurs. Since the time of Bernard it has often been assumed that in diabetes some disturbance of the central nervous system might be one of the factors operating through the liver to bring about this condition. A more probable explanation of the congestion of the liver in such cases appears to me to be the increased work thrown on the organ by the consumption of the large quantities of food and drink necessitated by the condition itself.

Symptoms.—The symptoms of active congestion group themselves into two classes: those connected with the condition, gastro-intestinal or other, with which the congestion is associated; and those referable to the disturbances in the liver itself. The common symptoms are those of gastric or gastro-duodenal catarrh—headache, malaise, loss of appetite or sickness, bitter taste in mouth, coated tongue, constipation—to which are added a sense of discomfort, weight, or even actual pain and tenderness *over the region of the liver itself; the patient at the same time usually presents the muddy complexion and the yellow eyes so characteristic* of liver disorder. The pain and discomfort over the liver are aggravated by pressure or by movement; they may be affected even by pressure of the clothes. Not infrequently the pain is referred to the right shoulder.

The liver is found appreciably enlarged; it projects below the costal margin, and it is tender to touch.

There is usually a slight degree of jaundice; in the group of cases depending on toxic influences it may be considerable, even intense.

The urine is high-coloured, concentrated, of higher specific gravity than normal, and usually loaded with urates; not infrequently also it contains uric acid crystals. Bile pigment is usually absent, except in the presence of jaundice.

The nervous disturbances are not the least prominent and disagreeable, including as they do not only headache and feelings of giddiness, but also great irritability of temper and mental depression.

Clinical varieties.—According to the severity and duration of the attack, two varieties are to be recognised—*acute*, met with in fevers, and marked by much constitutional disturbance; *chronic*, where the symptoms are more those of disorder of digestion, connected with long-standing habits as to food, drink, and exercise.

Morbid anatomy.—The anatomical changes found after death in cases of active congestion are ill marked. The liver is swollen, enlarged, dark in colour; and on section its vessels are found very full of blood. This overfilling is not limited to the central portions of the lobule, as in the "cardiac liver" (chronic congestion). The lobules may show some appearances of fatty change; but the mottling (nutmeg appearance), so characteristic of the cardiac liver, is not seen. On microscopic examination the liver-cells are swollen and often fatty; or they show some degrees of parenchymatous degeneration and cloudy swelling.

The changes as a whole are significant of over-activity, and differ from the atrophic and pressure changes presented by the "nutmeg" liver.

Diagnosis.—The diagnosis rests on a concurrence of symptoms of gastro-intestinal disturbance with enlargement of the liver, and pain and discomfort in the region of that organ.

Prognosis.—The condition is not dangerous in itself. It derives its importance from its causes.

Treatment.—The indications in treatment are mainly two: (*a*) To correct the habits of life on which the condition mainly depends; (*b*). To remove the gastro-intestinal conditions and the associated hyperæmia which prevails throughout the portal system.

(*a*) If the error be one of excess the food must be smaller in quantity, less bulky, and less stimulating in character, and the intervals between meals longer. In the choice of food regard must be had to the *stomach, and only such food given as will be readily digested without giving rise to irritating products.* Sauces and all dishes containing overheated fats, such as entrées, pastries, and the like, should be avoided. Fat in any form should be taken sparingly. The safest meats are those roasted, or, in the case of fish, boiled or broiled.

If the immediate cause of the congestion be alcoholic excess, as it often is, alcohol in every form should be cut off for the time being. If alcohol be only one of the factors it should be taken in strict moderation, and only with meals. Indeed, the quantity of liquid of any kind taken with meals should be small; liquids are better taken on an empty stomach between meals. Our object in these measures is to avoid undue dilution of the gastric juice during active digestion—to restrict the inflow of blood into the portal system and lessen the amount of digestive work to be done.

(*b*) In carrying out these measures we are doing much to carry out the second indication of treatment; for by regulation of the diet we diminish and get rid of the gastric catarrh, with the associated hyperæmia throughout the portal tract. Much can also be done in this direction by use of medicines, such as bismuth with alkalies and bitter tonics given before food; or dilute acids, especially nitro-hydrochloric acid with nux vomica, after food.

But our chief means of diminishing the hyperæmia throughout the portal system is free depletion of this system by purgatives. At the same time the patient must be led to take more exercise. For the former purpose we prescribe the various saline purgative mineral matters—Carlsbad salts, preferably in effervescing form, Marienbad, Homburg, or Johannis—taken on an empty stomach in the morning, with an occasional pill at night time, containing one or more of such drugs as podophyllin, mercury in the form of blue pill, aloes or aloin, nux vomica, or rhubarb (compound pill). How much such measures are calculated to relieve the condition is shown incidentally in cases where a copious bleeding from piles is immediately followed by great relief to the more distressing liver symptoms, possibly even by appreciable diminution in size of the liver itself.

When, as often happens, the liability to such congestive attacks becomes a habit of life, the treatment becomes a much more difficult task. In addition to the foregoing measures, it is in such cases that great benefit is derived from periodic visits to such watering-places as Homburg, Carlsbad, Marienbad, or Vichy. The benefit thus obtained is partly due to the use of the various purgative waters, partly also to the more regular life and the more restricted diet to which patients, otherwise unamenable to advice, more readily conform.

REFERENCES

1. CHAUFFARD. "Maladies du Foie," *Traité de médecine*, vol. iii. 1892.—2. KELSCH and KIENER. *Traité des maladies des pays chauds*, Paris, 1889, p. 172.—3. SENATOR. *Berl. klin. Woch.* 1872.

Passive Congestion.—*Synonyms.*—*Nutmeg liver; Cyanotic atrophy of liver; Cardiac liver.*—**Definition.**—A pathological condition consisting in an excess of blood within the liver, caused by obstruction to the outflow of blood from the organ, in the great majority of cases as the result of cardiac disease; characterised at first by enlargement of the liver, in the later stages by shrinking and atrophy, with symptoms of impeded portal circulation.

Etiology.—This form of congestion differs essentially from the one already considered in being of purely mechanical origin. It is the result of impeded outflow of blood from the hepatic veins, consequent on backward pressure of blood in the inferior vena cava. The conditions which lead to this are such as interfere with the free passage of blood through the heart, and include, therefore, all those lesions, whether of cardiac or of pulmonary origin, which tend to functional incompetence of the right side of the heart. Of the cardiac conditions the most common is mitral disease, both dilatation and stenosis, especially the latter; but all other heart lesions, whether valvular or inflammatory, and degenerative alterations of the cardiac muscle, tend to produce this condition in proportion as they throw increase of work upon the right side of the heart, and ultimately weaken it.

Certain *pulmonary* conditions, in so far as they impede the circulation through the lungs and throw increased work upon the right side of the heart, also favour its production. The most common of these is general emphysema with chronic bronchitis. Other conditions are chronic interstitial pneumonia, congenital atelectasis, pneumonia, atrophy of lungs, and compression of lungs, whether by pleuritic exudations (especially of the left side) or by intrathoracic tumours (aortic aneurysms, mediastinal tumours).

Lastly, in quite exceptional cases the obstruction to the outflow of blood from the liver may be produced by more local lesions—constriction of the hepatic veins themselves as the result of chronic periphlebitis, or narrowing of the vena cava above the junction of the hepatic veins by tumours in this region (aneurysms, enlargement of glands), or extensive effusions into the left pleural cavity. The latter may push the mediastinum so much to the right as to bend the vena cava almost at a right angle.

Morbid anatomy.—The result of these various changes is an engorgement of the venous system of the body which tends especially to affect the liver, as the organ nearest the obstruction. The liver is engorged with blood and greatly enlarged; and inasmuch as the cause of the hyperæmia is usually permanent (for example, valvular disease), the hyperæmia itself is permanent, and ultimately leads to permanent structural changes. The engorgement of the vessels especially affects the capillaries in the centre of the lobule in immediate relation with the hepatic veins. They become greatly dilated, the liver-cells around are shrunken and atrophied by pressure, and usually contain much yellow blood pigment. The centre of the lobule thus presents a deeply congested pigmented appearance; and, inasmuch as the cells in the outer zone of the lobule are usually fatty, there is a marked contrast between the congested and the fatty zones. On section the liver thus shows a mottled appearance, like that of a nutmeg—hence the title "nutmeg liver."

In course of time other secondary changes ensue. The increased pressure leads to an increase of the connective tissue in the centre of the lobule, and eventually to a well-marked induration and shrinking of the liver substance. In the later stages of the condition, then, enlargement gives place to an atrophy and induration of the organ (cyanotic atrophy, or induration of the liver).

Symptoms.—The symptoms accompanying the above condition are mainly those of the cardiac or pulmonary condition giving rise to it; but there are in addition others more directly due to the liver itself. Chief among these is the *enlargement of the liver*, sometimes recognisable only by percussion, at other times so great as easily to be made out by palpation. In severe cardiac cases it may be so great as to form a prominent swelling on the right side of the abdomen, extending a hand's-breadth or more below the costal margin; not infrequently in early stages of congestion it pulsates synchronously with the heart's beat, but as the congestion becomes chronic, and the liver hardens, this phenomenon disappears.

The patient experiences a great *feeling of fulness or tension* on the right hypochondrium, aggravated by external pressure or forced respiratory movements, usually also much increased by lying upon the left side.

Gastro-intestinal symptoms are usually more or less marked. They are the result of the congestion produced throughout the whole portal tract by the obstruction to the outflow of blood from the liver. They take the form of disturbed digestion and impaired peristalsis, sometimes also of hæmorrhoids.

Ascites is also common. In the early stages it is only a part of a general dropsy. In the later stages, when atrophy and induration of the liver occur, it may be the direct result of the state of the liver. A degree of ascites, then, out of proportion to the general dropsy may indicate cyanotic induration of the liver.

A more definite symptom of liver disorder is the occurrence of *jaundice*. A certain degree of jaundice is very common in severe cases, causing, with the cyanosis, the peculiar dusky green discoloration of face which such patients present. It is the result of obstruction, occasioned by congestion and tumefaction of the tissues and catarrhal swelling of the epithelium of the bile-ducts.

The *course and duration* of these symptoms depend entirely on that of the conditions which give rise to the obstruction. In heart disease they are gradually established; and they vary from time to time according to the capacity of the right ventricle. It is only when the condition has been so long established as to lead to induration and atrophy that it may be said to have an independent existence, causing, it may be, more or less permanent ascites. Short of this the condition cannot be said to be an independent one, or in itself dangerous to life.

Treatment.—The treatment is mainly, of course, that of the cardiac or pulmonary condition which gives rise to it. At the same time the local symptoms can be much relieved by diminishing the portal congestion, either indirectly by cathartics, or more directly by applying half a dozen leeches over the liver.

To fulfil the first indication, great benefit will be got by occasional doses of calomel, or of smaller and more regular doses of blue pill, often in combination with digitalis. When given in repeated doses calomel acts in such cases not only as a cathartic, but as a powerful diuretic also. Vegetable aperients are also useful; podophyllin, rhubarb, aloes: also the various mineral salts, such as sulphate of soda, sulphate of magnesia, or the mineral waters containing them—Carlsbad, Marienbad, Homburg, and others.

JAUNDICE

The General Pathology of Jaundice

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Summary.

Definition.—A general condition symptomatic of disorder either of the liver alone (hepatogenous jaundice), or of the liver and the blood in association (hæmo-hepatogenous jaundice); characterised by yellowish discoloration of the tissues with bile pigment, the excretion of bile pigments in the urine with or without bile acids; and by various general symptoms referable, in simple cases, to disturbances of gastro-intestinal and liver functions, in more severe cases, to disorder of the blood as well as of the liver (fever, cerebral symptoms, hæmorrhages). Caused by absorption of bile from the bile passages as the result of impeded obstructed outflow.

Introductory.—The subject of jaundice has long had a peculiar interest alike for clinician and pathologist. It is one of the few subjects in connection with which a theory has long occupied a prominent position in all treatises on medicine. In the present article it is proposed to discuss its general pathology in the light of much recently acquired knowledge. It is interesting to note that another well-marked disease, the general pathology of which has excited a like interest, namely, diabetes, like jaundice is connected with disorder of the liver.

The theory of jaundice has not been exempt from the liability to change incidental to all theories. The changes it has undergone from time to time are interesting in that they serve to denote for each successive period the extent of knowledge regarding the relations of the liver and the blood. In its obstructive varieties one of the most easily understood of conditions, in other varieties, apparently unconnected with obstruction, it has long been a fruitful subject of speculation: by general consent, however, the latter varieties have been ascribed to disorder of the blood rather than of the liver itself.

That jaundice does arise in connection with certain disorders of the blood is a very old observation. But it is only within the present century that the association has been investigated. The connection of the two disorders is indeed frequently referred to as far back as the time of Galen; but such observations indicate little more than the prevailing opinion of ancient writers that disorder of the blood is the primary cause of most diseases.

In later times, when this criticism does not so closely apply,—at the end of last century and the beginning of the present,—it is to be noted that the chief authors discuss the possibility of a form of jaundice unconnected with obstruction in the liver, though they are very far from admitting its probability. It is clear, however, that the jaundice connected with blood disorder was clinically well known to them Thus Reil (1782) gave a long description of its chief features under the title "Polycholia," with rules for distinguishing it from ordinary jaundice. Saunders also (1809) recognised that jaundice might be associated with a redundant secretion of bile and be independent of biliary obstruction; as, for example, the jaundice of yellow fever. He even went so far as to admit that in certain morbid states the blood might acquire a bilious appearance independently of absorption or regurgitation of bile from the liver, thus practically anticipating the later hæmatogenous doctrine of jaundice. But that he held such a mode of origin of jaundice to be unlikely is plain from his subsequent conclusion, that "in every case of jaundice bile must be secreted and carried into the blood-vessels"; in other words, the jaundice is essentially of obstructive origin. And, indeed, it would have been strange if the importance of obstruction as a cause of jaundice had been overlooked by Saunders; since he was the first to demonstrate by experiment the channels by which, after obstruction of the bile-duct, the absorption of bile takes place; namely, the lymphatics. He ligatured the bile-duct, and afterwards was able to trace the lymphatics of the liver distended with bile up to their junction with the thoracic duct.

Still later (1827) Cullen also rejected any other mode of origin of jaundice than that of absorption of bile already formed by the liver. He distinguished two ways in which jaundice might arise in this way: namely, (i.) obstruction to the flow of bile into the duodenum; and (ii.) reabsorption of bile from the alimentary canal when it had accumulated there in an unusually large quantity. How far this accumulation could take place, and under what circumstances it occurs, he could not clearly ascertain; he considered, however, that jaundice was seldom produced in this way.

Similarly most other writers about the end of last century taught that the doctrine of jaundice from absorption was the only trustworthy one; jaundice was essentially obstructive in its nature. And it may be stated generally that, up to the end of the first quarter of the present century, the state of knowledge did not permit any further deduction. It was recognised that there are certain forms of jaundice not clearly traceable to obstruction, but difficult to account for on any other supposition.

I. Frerichs' hypothesis.—During the second quarter of the century the view, hinted at by Saunders, that jaundice might arise from pure disorder of the blood, independently of obstruction, began to take more definite form. It was not, however, till 1858 that any serious attempt was made to define more precisely what such a view implied—to indicate whether the fault lay in the blood or in the liver. The first attempt of this kind we owe to Frerichs, whose results appeared to show that the fault lay in the blood, and that the jaundice was due to accumulation of bile pigments imperfectly oxidised in the blood.

Frerichs distinguished two possible causes which might lead to an accumulation of bile constituents in the blood: (i.) increased absorption of bile into the blood, whether from obstruction in the bile-ducts, or from abnormal diffusion of bile into the blood capillaries of the liver under conditions in which the blood-pressure within the liver was diminished; or (ii.) diminished consumption or metamorphosis of the bile constituents absorbed into the blood under normal circumstances from the alimentary canal. Chief among these constituents and the precursors of the bile pigments he considered to be the bile acids; for he found that, by the action of sulphuric acid on bile acids, various pigments or chromogens were formed resembling in many respects the pigments of the bile, especially in their behaviour towards Gmelin's reagent. On the basis of these observations he conceived the normal fate of the bile acids absorbed from the intestine into the blood to be that they underwent a similar change in the blood, and were converted into bile pigment; and that this in turn became oxidised within the blood into urinary pigment. Any interference with this normal oxidising process would thus necessarily lead to an excess of bile pigment in the blood; and in this way a jaundice might arise quite independently of any obstruction.

Frerichs made certain other observations which seemed strongly to support his views. For he found that if bile salts were injected into the blood of dogs they disappeared, while bile pigment appeared in the urine.

According to this view, then, the fault lay entirely with the blood, which did not oxidise the bile pigment normally absorbed into it; and jaundice might arise either from increased absorption of bile into the blood, or from diminished metamorphosis of bile absorbed in normal quantity.

II. Kühne's hypothesis.—"*Hæmatogenous Jaundice.*"—Frerichs' important observations on the appearance of bile pigment in the urine after the injection of bile salts into the blood was soon confirmed by Kuhne (1858). But so far from lending support to the views of Frerichs, Kuhne's observations led, curiously enough, to the establishment of a radically different theory of jaundice. Kühne showed that the explanation of the appearance of bile pigment in the urine, after injection of bile salts, was very different from that supposed by Frerichs. Kuhne found that if, instead of bile salts, he injected hæmoglobin into the blood, bile pigment still appeared in the urine. He concluded, therefore, that the bile acids did not become directly converted into bile pigment, as Frerichs had supposed, but that they liberated the hæmoglobin of the corpuscles, and that this was subsequently transformed into the bile pigment. On the ground of these observations he formulated the doctrine that all agents capable of liberating an excess of hæmoglobin in the blood were capable of inducing icterus—at any rate to a degree sufficient to cause bile pigment to appear in the urine.

The important point established by these observations of Kuhne was that hæmoglobin is the source of the bile pigments. It is not too much to say that this observation marked a new era in the history of the subject; later observations have but confirmed its truth. Very soon it received support from Virchow's discovery, in and around old extravasations of blood, of crystals of hæmatoidin, a pigment closely resembling bilirubin if not identical with it. As the hæmoglobin of extravasated blood could undergo this conversion it was reasonable to suppose that under certain circumstances it might undergo a like transformation in the blood. Taken with the foregoing observation that bile pigment appears in the urine after the injection of hæmoglobin into the circulation or on its liberation there, the evidence seemed, indeed, conclusive that such a transformation had taken place, and this, too, directly in the blood without the intermediation of the liver. The liver was not concerned in the process. Such jaundice must be purely "hæmatogenous"—in no sense obstructive.

The doctrine of a hæmatogenous jaundice thus formulated very soon received what appeared to be strong support from the clinical side. Leyden's important observations (1866) appeared to confirm the view that the blood, and not the liver, is the tissue at fault. He found that in obstructive jaundice bile acids are always present in the urine with bile pigment; whereas in the jaundice of pyæmia and allied blood disorders they are not to be found. As the bile acids are formed by the liver, their absence from the urine in such cases seemed to indicate inaction of the liver and that the bile pigments present in the urine had not been formed by the liver, and, consequently, that this jaundice is not due to obstruction.

As a matter of fact the accuracy of Leyden's observation was very soon called in question. But it fitted in so completely with Kuhne's doctrine that his teaching soon gained a very general acceptance, and has held its ground even up to the present time. The detection of bile acids in the urine has been accepted as a sign of obstructive jaundice; their absence as a sign of so-called "non-obstructive" or "hæmatogenous" jaundice.

Chief among the supporters of the doctrine of a hæmatogenous jaundice at various times have been Leyden in Germany, Gubler in France (1857), Budd (1845), and Harley (1865) in this country; and among recent writers it has received qualified support from Bristowe (1890) and Fagge (1891).

The class of diseases to which it was held to apply were such as pyæmia, typhoid fever, pneumonia, and febrile jaundice generally; the jaundice following burns and scars; that following the injection of water, pyrogallic acid, or other destructive agents into the blood; and that of malaria, paroxysmal hæmoglobinuria, and other diseases marked by blood-destruction.

The doctrine always failed, however, to gain acceptance from Frerichs in Germany, or Murchison in this country (1868); and it was likewise deemed insufficient by Wickham Legg (1880). It was indeed very soon rejected as insufficient by the very observer to whom, in the first instance, it owed its name, and who is often regarded as its founder. Virchow it was who first suggested the name "hæmatogenous" to describe this kind of jaundice; and, as we have seen, his own observations lent no little support to the doctrine. Yet, whatever his early views, his later opinion undoubtedly was that a purely hæmatogenous origin of jaundice in any form is extremely improbable. Even in such diseases as pyæmia or pneumonia he held that obstruction, due, it may be, to catarrh of the bile-ducts, plays a very prominent part.

It will presently be seen how fully this scepticism of the great pathologist has been justified by the most recent work on the subject. Before considering this matter, however, it will be convenient to refer to another hypothesis, having certain close relations to the hæmatogenous doctrine; namely, the theory of "jaundice by suppression."

III. The suppression hypothesis.—According to this hypothesis the jaundice, unattended by obstruction, is due to a suppression of the biliary secretion as the result of some morbid action of the liver itself. "The biliary ingredients are not eliminated, and consequently accumulate in the blood" (Harley). This is the oldest theory of all. At what time, indeed, it took origin is not clear. A doctrine identical with it was expressed by Boerhaave (1757) and by Morgagni; but it is probably much older than their writings. Such a doctrine was in strictest keeping with the early knowledge of the functions of the liver, its chief function being compared to that of a sieve which strains off the bile from the portal blood (Glisson, 1659).

According to the modern version of this hypothesis, biliary secretion can be retarded or even totally arrested, for instance by nervous influence, without any structural alterations in the liver-cell. The liver can "strike work" and refuse to secrete bile, and the result is jaundice. It is claimed for this hypothesis that it rests on a basis of pathological facts, and in support of its accuracy special importance is attached to certain cases of obstruction described by Moxon and others, where the gall-bladder and larger bile-ducts behind the point of obstruction are found filled with colourless mucus free from all trace of bile.

The class of cases to which it is applied by its supporters includes—(i.) Those in which jaundice occurs as the result of sudden mental emotion or other severe nervous disturbance; (ii.) Most of the cases in which it occurs in connection with disorder of the blood, such as typhus, enteric fever and infective diseases generally, icterus gravis, yellow fever, acute yellow atrophy, snake poisoning and phosphorus poisoning—cases of much the same class, indeed, as those to which the hæmatogenous doctrine applies. And, indeed, at some points the two doctrines are closely related. They differ, it is true, in this respect, that while according to the hæmatogenous doctrine the whole fault lies with the blood, the only fault ascribed to the liver being that it cannot dispose of all the hæmoglobin supplied to it, according to the suppression theory, on the other hand, the fault lies entirely with the liver, the function of which is arrested. Nevertheless the two views have this in common, that both assume the bile pigments to be formed from hæmoglobin within the blood, and merely to be excreted by the liver; and, consequently, that jaundice is liable to occur if at any time there be an excess of hæmoglobin in the blood on the one hand (hæmatogenous), or an arrested activity of the liver on the other (suppression theory). In disease, as it happens, both factors are often combined, since the poison which acts injuriously on the blood also acts injuriously on the liver. Hence it is impossible to separate the two processes entirely; since, but for the facts in support of the hæmatogenous doctrine, the suppression theory would have little or nothing to recommend it.

The theory of jaundice by suppression has received support from Andral (1839), Budd (1845), Sir Thomas Watson (1867), Bamberger (1857), Trousseau (1865), Liebermeister (1864), Harley (1880), and Moxon (1873). The last-named observer, indeed, went so far as to apply the theory to obstructive forms of jaundice no less than to those where no obvious obstruction could be found. In obstructive jaundice he considered the yellowness to be caused by suppression of the secretion, and not by absorption of bile already formed; unless as an unimportant incident of the earlier stages of the jaundice. "We may deny that re-absorption of bile is a cause of jaundice." In extending the doctrine of suppression thus far, Moxon, I think, stands alone ; its other supporters are content to apply it to the cases where no obvious obstruction can be found.

Consideration of foregoing doctrines.—Of the three doctrines just considered, the only one which has contributed definitely to our knowledge is the hæmatogenous doctrine.

Frerichs' teaching has contributed nothing. The bile pigments are not derived from bile acids as he supposed ; and the oxidation processes, to the arrest whereof the accumulation of bile constituents in the blood was ascribed, have as problematical an existence now as ever they had.

The suppression doctrine took origin at a time when the excretion of bile was supposed to be the sole function of the liver. In this case, if the liver cease to act, the bile constituents accumulate in the blood. We now know that the chief constituents of the bile do not pre-exist in the blood, but are formed by the liver.

The hæmatogenous doctrine, on the other hand, is based upon a fact of definite importance, namely, that the bile pigments are derived from hæmoglobin, and not infrequently appear in the urine after a liberation of hæmoglobin in excess. Where this doctrine proved wanting was not in facts, but in the interpretation of them. It assumed that the conversion of hæmoglobin into bile pigment takes place within the blood, and upon this assumption the doctrine depended. Indeed, the occurrence of jaundice in connection with increased blood-destruction was conversely adduced by the physiologist as an argument in favour of the purely hæmatogenous origin of bile pigment.

VARIOUS FACTORS IN THE PRODUCTION OF JAUNDICE

A. Hæmatogenous origin of bile pigment ("Hæmatogenous jaundice").—*Possibility of a hæmatogenous origin of bile pigment.*—Even now it may be said that, although the evidence against such a mode of origin largely preponderates, a certain, albeit limited, amount of evidence is still adducible in its favour. For there still remain a few observations which lend support to the view that bile pigments may be formed independently of the liver-cell. On the one hand it has been shown by the important experiments of the two German observers, Minkowski and Naunyn (1886), that increased formation of bile pigments (induced in their experiments by exposing the animals to the fumes of arseniuretted hydrogen, and thereby causing great destruction of blood) goes hand in hand with the appearance of numerous pigment-holding cells in the capillaries of the liver, some of them containing bile pigment. They conclude that within these cells, which, be it noted, are not liver-cells, but ordinary leucocytes and connective-tissue cells lying in the capillaries of the liver, the hæmoglobin is transformed into bile pigment, which afterwards is simply excreted by the liver-cells.

Similarly another observer, Löwit, finds that in frogs it is the normal fate of red corpuscles to be taken up by cells of the blood (leuco-

cytes), and that within these their hæmoglobin becomes converted into bile pigment in the liver, spleen and bone-marrow.

Lastly, Neumann has recently studied the mode of origin of hæmatoidin—the crystalline pigment, as we have already noted, identical with bilirubin—and concludes that its formation from hæmoglobin is a simple chemical process independent altogether of the activity of cells of any kind, whether leucocytes or any other.

As the result of my own observations on formation of hæmatoidin in extravasated blood, I came to similar conclusions (1886).

Recently (1896) Dr. Auld concludes from his experiments that the jaundice following the action of certain poisons (phenylhydrazin and metaphenylendiamin) is due to pigments formed in the spleen and carried through an inert liver into the general circulation.

These observations derive their importance in relation to jaundice, not so much from their number as from their nature. If bile pigments, or allied pigments like hæmatoidin, can be formed directly from hæmoglobin, whether by the action of leucocytes or other non-hepatic cells, or even altogether independently of cell action, there is no a priori ground why, as the hæmatogenous doctrine contemplates, a similar transformation should not take place in disease, and set up certain forms of jaundice otherwise difficult to explain. The possibility of an extrahepatic origin of bile pigments or allied pigments is thus not to be gainsaid. Nor is the significance of this admission materially lessened when it is argued that it is unlikely in the highest degree that this formation should ever take place to such an extent as to occasion any marked degree of jaundice; for most of the forms of jaundice with which the hæmatogenous theory concerns itself are not marked by their severity: they are often but slight in degree, as, for example, in pyæmia; they are denoted by a slight yellowness of skin or conjunctiva, together with the presence of bile pigment in the urine, rather than by any pronounced discoloration. Moreover, in that variety of jaundice or yellow discoloration accompanying the absorption of large extravasations of blood, and marked by the presence of much urobilin pigment in the urine ("urobilin icterus"), it is possible from the small quantity or entire absence of bile pigments in the urine that other colouring derivatives of hæmoglobin may be the cause of the yellow discoloration.

To sum up, then, it may be repeated that so far as the hæmatogenous doctrine of jaundice is based on the possibility of the formation of bile pigments, or allied coloured derivatives of hæmoglobin, directly from hæmoglobin without the agency of the liver-cells proper, some basis for this doctrine still remains.

The liver the chief seat of formation of bile pigment.—On the other hand, so far as it rests on the assumptions that the bile pigments are normally formed within the blood, and that the liver merely excretes the bile pigment conveyed to it, the hæmatogenous doctrine I consider to have been deprived by later observations of all basis whatever. For the important experiments of Stern on pigeons (1885), and of Minkowski *and Naunyn on geese (1886), have conclusively shown, for warm-blooded* animals, what Kunde and Moleschott's experiments long ago showed for the cold-blooded (frogs), that the removal of the liver under the precise conditions which ought to favour a hæmatogenous jaundice is not followed by jaundice at all. These observers showed that, if in the healthy goose a liberation of hæmoglobin be induced by the inhalation of arseniuretted hydrogen, bile pigments appear in quantity in the urine; not followed by free hæmoglobin unless the destruction be great. If, however (under similar conditions), the liver be cut off from the circulation, either by excision or by ligature of all its vessels, the hæmoglobin appears directly in the urine, without any bile pigments. In the absence of the liver the hæmoglobin was not converted into bile pigment as was the case in health. If the bile pigments were normally formed from free hæmoglobin within the blood, the removal of the liver ought not to have appreciably affected their formation; still less should their formation be practically arrested. These results warrant the conclusion that, under normal circumstances, it is within the liver, not within the blood, that hæmoglobin is converted into bile pigment.

This conclusion would lose some of its force and significance in the present relation if, as Minkowski and Naunyn seem to think, it is the leucocytes of the capillaries, not the liver-cells, that are chiefly concerned in transforming the hæmoglobin into bile pigments. But in my opinion there is strong reason for doubting the correctness, not of their observations, but of their interpretation of them. I have carried out a large number of experiments, involving destruction of blood, both in birds (pigeons) and in mammals (rabbits, dogs, cats), and paid special attention to the significance and importance of pigment cells within the capillaries of the liver. And my observations lead me to attach little or no significance to these cells in respect of the formation of bile pigment; and for these reasons—(i.) In certain animals (rabbit) the presence of pigment cells within the capillaries of the liver is the exception, not the rule; yet bile pigments are formed in normal quantity. (ii.) If increased blood-destruction be induced by suitable agents —as, for example, by distilled water or toluylendiamin—a largely-increased formation of bile pigments occurs, without any pigment cells necessarily appearing in the capillaries (rabbit). (iii.) Even if under such circumstances pigment cells appear in the capillaries of the liver (dogs, pigeons after toluylendiamin poisoning), their number is far too few to be held accountable for the largely increased formation of bile pigment which then occurs. This latter fact is admitted by Minkowski and Naunyn themselves; and it serves in itself to do away with much of the special significance they have attached to the occurrence of cells, admittedly few in number, containing what they regarded as biliverdin. Further, they admit that they could not find any evidence of the formation of biliverdin within the pigment cells of the spleen—a curious circumstance if it be within such cells that hæmoglobin is converted into bile pigment.

As to the actual significance of cells containing blood pigment within the capillaries of the liver, my observations lead me to very different conclusions. It is not the hæmoglobin stored within such cells that is the source of the bile pigments, but the hæmoglobin which passes into the liver-cell itself. My observations point strongly to the conclusion that in health the transformation of hæmoglobin into bile pigment is a purely hepatic function—that is, a function discharged by the liver-cell proper.

The basis of facts on which the hæmatogenous doctrine rests is thus narrowed almost to vanishing-point. The only basis it retains is the somewhat slender one supplied by the observations above cited, namely, that the formation of hæmatoidin from hæmoglobin is a purely chemical process independent of cell activity. On the ground of this observation Neumann and Lowit remain firm supporters of the hæmatogenous doctrine of jaundice. Slender as its basis admittedly is, this doctrine would nevertheless remain the most reasonable explanation to be offered of the obscure forms of jaundice connected with blood disorder, but for another series of observations, throwing an entirely fresh light on the whole subject, that have next to be considered.

B. Jaundice produced by poisons.—*Stadelmann's observations—Hæmo-hepatogenous jaundice.*—The observations referred to are those of Stadelmann (1881-1883). They show, for the group of cases to which the hæmatogenous doctrine was supposed specially to apply, cases, that is, of jaundice accompanying an increased destruction of blood, that the jaundice is due to obstruction caused by well-marked changes in the character and consistency of the bile.

The action of toluylendiamin.—The study of one drug in particular, toluylendiamin, has proved of special interest in this relation. This drug, when injected into dogs, possesses the peculiar action, first noted by Schmiedeberg, of causing intense jaundice. Stadelmann, at the request of Schmiedeberg, undertook its closer study. He found that its action caused well-marked changes in the bile differing at different stages. In the first stage (beginning about 2 hours after the injection, and lasting 12 hours) the bile is increased in quantity and very rich in bile pigments. In the second stage (beginning about the 14th hour and lasting 60-70 hours) it becomes greatly diminished in quantity, gradually loses all the characters of bile, and assumes those of an extremely viscid colourless mucus. At the end of this time it begins gradually to assume its normal character, and there is again an increased excretion of bile pigments. The jaundice begins towards the end of the first stage, becomes very pronounced during the second, and gradually passes off during the third.

A notable feature of the jaundice thus occasioned is the behaviour of the bile acids. During the first stage, when the bile pigments are increased, the bile acids are diminished. Hence their appearance in the urine does not coincide with that of the bile pigments; for while the latter are present in quantity 15 to 20 hours after the injection, the bile acids do not appear till about the 22nd, 31st, or 48th hour; in the next

24 hours they reach their maximum, diminish during the following 24 hours, and then disappear altogether.

Afanassiew supplemented these observations in one important particular by showing, what Stadelmann at first failed to recognise, that the drug exercises a markedly destructive action on the blood—an observation which appeared to supply the missing clue to the explanation of the jaundice.

According to Stadelmann the sequence of events is as follows: The drug causes a destruction of blood; the hæmoglobin liberated leads to an increased formation and excretion of bile pigments (polychromia); this is attended by an increased viscidity of the bile, which, at the low pressure at which the bile is excreted, causes a temporary obstruction, with reabsorption of the bile and jaundice; and, finally, when the action of the drug exhausts itself, the bile gradually loses its viscid character, the flow of bile is re-established, and the jaundice disappears. A jaundice which thus had every appearance of being essentially hæmatogenous, even in respect of the absence of bile acids from the urine in the first instance, at a time when bile pigments were present in quantity, was thus shown to be really of obstructive origin, and to depend upon alterations (increased viscidity) in the character of the bile.

The same observer found, moreover, that a similar explanation applies to other varieties of jaundice associated with increased destruction of blood.

Thus *poisoning with arseniuretted hydrogen* occasions a remarkable concentration of the bile—the gall-bladder and bile-ducts being filled with a thick, viscid bile frequently containing large quantities of amorphous sediment, as well as numerous crystals of bilirubin. The increase of bile pigments in the bile is very marked; absolutely it amounts to as much as 3½ times the previous amount, and relatively is still larger (20 times) as the quantity of bile is reduced 5½ times. Yet, notwithstanding this striking increase in bile pigments, the bile acids are in no way increased, indeed they are reduced to one-tenth their normal amount—the same disproportion between bile pigments and bile acids being thus shown as in the case of toluylendiamin poisoning.

In the case of this agent Stadelmann conceives that "the destruction of the blood is the occasion of the jaundice—only, however, through the agency of the liver, which produces an abnormal bile in consequence of the abnormal blood conveyed to it."

Lastly, a similar explanation would appear to apply to the jaundice occasionally met with in conditions of hæmoglobinæmia, whether induced by injection of free hæmoglobin or of distilled water. Stadelmann's observations show that changes in the bile are induced thereby, namely, increase of bile pigments, increased viscidity of bile and diminution of bile acids—changes similar in character, although by no means so marked in degree, as those produced by toluylendiamin or arseniuretted hydrogen.

The obstructive nature of toxic jaundice.—For the whole group of cases of jaundice accompanying increased destruction of blood, the foregoing observations show conclusively that the jaundice is really obstructive in its nature, albeit the obstruction be temporary in character, and dependent upon an increased viscidity of the bile induced by the changes in the blood. *It is really then hepatogenous, not hæmatogenous; but to signify its dependence upon the preceding blood changes it might be described,* as Afanassiew has proposed, by the term *hæmo-hepatogenous.*

The importance of this conclusion in relation to the pathology of so-called "non-obstructive" jaundice cannot well be over-estimated. For it will be obvious that the great majority of the conditions in which this variety of jaundice is assumed to occur—blood-poisoning, pyæmia, acute yellow atrophy, malaria, paroxysmal hæmoglobinuria, and so forth, are precisely those in which increased blood-destruction is either obvious or likely to be present.

Nor does their significance end here. The observations throw light not only on the class of cases formerly described as hæmatogenous, but also on those obscure forms of jaundice regarded as due to suppression. The jaundice attending *phosphorus poisoning* has long been adduced as an exemplary instance of a jaundice due to suppression of the hepatic function. And yet Stadelmann's observations appear to show that this form of jaundice depends upon bile changes similar in character to those above described, although much slower in production.

Ten hours after administration of phosphorus the bile begins to be darker in colour; the bile pigments are increased by one-half; the bile acids are diminished. For the next 24 hours these conditions persist, and no jaundice is manifested. Then the bile begins to change its character; it becomes clearer, more mucoid, and much diminished in quantity (one-fifth); the bile pigments fall to one-half or one-third of their normal amount, and the bile acids are even more reduced (0·1, 0·15, or 0·7 instead of the normal 1·96). At this stage jaundice appears and slowly reaches its maximum about five days after the administration of the poison. The jaundice then slowly disappears, its disappearance being marked by an increased excretion of bile pigments doubtless derived by reabsorption from the tissues. The bile acids still remain in defect for some days longer; and it is not till the tenth or eleventh day that they once more regain their normal amount.

Cause of the obstruction.—The foregoing observations show that the obstruction is due to increased viscidity of bile. And as this change appears to be an important factor in all cases of jaundice connected with blood disorder, it becomes a matter of importance to determine the precise cause of it. The matter has been worked out more especially in connection with one drug—toluylendiamin. The jaundice produced by this drug has a peculiar interest; so intense is it, and so regular in its occurrence. In large doses it reproduces all the features of a severe jaundice, with fever, and swelling of spleen and liver; such as we meet with clinically, for instance, in severe forms of icterus gravis, Weil's disease, or yellow fever.

Three different opinions have been advanced to account for the obstruction in the bile-ducts occasioned by this and similar poisons.

(*a*) Afanassiew considers the chief factor to be the compression of the smaller bile capillaries from without. As the result of the action of the drug, *he finds dilatation of the blood-vessels and lymphatics of the liver*, and a blocking of the capillaries with altered red corpuscles. He believes that the drug exerts an irritant action on the liver, causing a hyperæmic and œdematous state of its tissues, and consequently a compression of the bile capillaries. Of this view it may be said that the jaundice is out of all proportion to the alleged mechanical cause, and that far greater dilatation of blood-vessels is met with—in congestion of the liver, and in other conditions, without the occurrence of any such obstruction.

(*b*) According to Stadelmann the chief factor is undoubtedly the increased viscidity of the bile, a change he conceives to be connected in some way with the increase of bile pigments (polychromia). In his view the jaundice might be most fittingly called "jaundice from polychromia." Besides this polychromia, he considers that there is probably another factor in some special action of the poison which leads to the secretion by the liver-cell of a more concentrated bile, too thick to flow away. He concedes to Afanassiew that possibly at the same time the liver-cells are affected, press upon the bile capillaries, and cause absorption of bile. He thus contemplates a number of possible factors; but he attaches the chief importance to one—the increase of bile pigments. It is clear, however, as I have shown elsewhere (16), that this increase cannot be the chief factor; if it were, the obstruction ought to be proportional to the increase of bile pigments. Stadelmann's own observations, indeed, show that this is not so. Jaundice may be most intense with only a slight (one-half) increase of bile pigments (toluylendiamin); while, on the contrary, it may be slight or absent with a very great (three or four-fold) increase (arsenious acid poisoning).

(*c*) The conclusion I draw from my experiments in this matter is that the cause of the increased viscidity of the bile is an extensive catarrh of the intrahepatic bile-ducts from their origin downwards. In severe cases this catarrh may extend into the duodenum itself, and there cause the most intense inflammatory swelling and congestion of the mucous membrane, beginning definitely at the orifice of the bile papilla; the viscid catarrhal mucus which covers its surface being of the same character as that exuding from the bile-duct itself. A duodenal catarrh is, however, not necessary to this production. For the jaundice occurs even when the bile-duct is cut away from the duodenum (as in dogs with biliary fistula). This catarrh is excited by the passage of bile containing the poison itself, or irritant products of it, along the bile-ducts. I found the poison in the bile increasing in quantity from the first hour onwards. The catarrh causes, to begin with, an increased viscidity of bile (1st stage); as it becomes more intense, catarrhal mucus fills the bile-ducts to the exclusion of bile pigments (2nd stage); and it then passes gradually off as the poison is eliminated (3rd stage).

The chief feature of this catarrh in ordinary cases appears to me to be not so much its high degree as its excretory origin; beginning, as it does, in the smaller bile-ducts. Under the low pressure at which the bile is secreted, a very slight catarrh, set up by the excretion of an irritant through the liver, may from its widespread character easily *set up obstruction enough to cause some reabsorption of bile and some degree of jaundice. The jaundice so occasioned is, I conclude, proportioned*, not to the amount of the accompanying blood-destruction (hæmoglobinæmia), nor to the increase of bile pigments (polychromia), but to the irritant character of the substance or substances excreted in the bile *A poison (or its products) is likely to cause jaundice in proportion as it is capable of exciting catarrh of the bile-passages during its elimination by the liver.*

Toxæmic as distinguished from duodenal catarrh of bile-ducts.—According to these observations, I recognise a "descending" as distinguished from a duodenal or ascending catarrh, as a cause of jaundice. This variety of catarrh of the bile-ducts may, as I have suggested, be called "toxæmic," to distinguish it from the ordinary duodenal origin of catarrh of bile-ducts which is assumed to arise and travel up the bile-duct from the duodenum. In this latter case the catarrh is supposed to create obstruction and to lead to jaundice by blocking the opening of the bile-duct with a plug of mucus. Only in this sense is it spoken of by Murchison; and this teaching as to the mode of origin of catarrhal jaundice has gained wide and general acceptance. Stadelmann also seems to have considered the duodenum to be the necessary starting-point of jaundice of catarrhal nature; for in his experiments, when the bile-duct was ligatured off from the duodenum, and yet the jaundice still occurred, he regarded this result as conclusive of the "non-catarrhal" nature of the obstruction. The possibility of a catarrh spreading, not upwards from the duodenum, but down the bile-ducts from their origin, seems not to have presented itself to his mind. And yet such a catarrh would obviously be of the first importance in the pathology of a jaundice connected with blood disorder and set up by poisons. I consider, indeed, that in all probability this is a more common origin of catarrh of the bile-ducts, and consequently a more common cause of jaundice, than catarrh ascending from the duodenum. Both varieties of catarrh—the toxæmic and the duodenal—imply the action of an irritant, the one exerted on the bile-ducts in the course of its excretion with the bile from above downwards, the other on the duodenum and the mouth of the bile-duct. Of the two the former is the more likely, from its widespread character, to produce an obstruction sufficient to cause jaundice. It is certain, at least, for the reason already stated, that in the case of jaundice due to poisons a duodenal catarrh is not necessary for the production of the jaundice. If it occur, and it is only in the case of severe poisons that it does occur, it is not primary, but secondary to a previous catarrh set up in the bile-ducts during the elimination of the poison.

C. The relation between jaundice and blood-destruction.—It has been seen that in nearly every case a notable feature of the blood disorder caused by these various icterogenetic poisons is an increased destruction variously manifested, whether by morphological changes in the blood, by increased formation of bile pigments derived from hæmoglobin, by presence of hæmoglobin in the urine (hæmoglobinuria), or by all these combined.

The *connection between increased liberation of hæmoglobin* (*hæmoglobinæmia*) *and jaundice* appears so close that, as we have seen, it formed in Kuhne's hands the basis of the hæmatogenous doctrine. In his view an excess of free hæmoglobin in the blood sufficed of itself to cause bile pigments to appear in the urine. And the later experiments of Tarchanoff and Stadelmann appeared to establish the connection more closely; the former always found bile pigment in the urine of dogs after injection of water or hæmoglobin into the blood; the latter found that under such circumstances important changes occurred in the bile, such as increase of viscidity, leading to temporary retardation in its flow and consequent absorption of bile pigments into the blood.

As I have shown elsewhere, the connection between hæmoglobinæmia and jaundice is neither so close nor so constant as at first sight appears On the one hand, there is some reason to doubt the constancy or frequency with which bile pigment is to be found in the urine under such circumstances. The results on which Kuhne's view is based have been obtained in one kind of animals only (dogs), and not invariably in them. Now, experiments on these animals are open to this great source of fallacy, that bile pigment is not infrequently present in the urine even of healthy dogs. And the experiments of Naunyn, as opposed to those of Tarchanoff, conclusively show that even in dogs marked hæmoglobinæmia—sufficient to cause hæmoglobinuria—does not necessarily cause bile pigments to appear in the urine Naunyn caused hæmoglobinuria by injecting hæmoglobin subcutaneously, yet in only two out of six cases did the urine react to Gmelin's test (bile pigment), and in both these cases the urine had given the same degree of reaction before the experiment.

In other kinds of animals, such as cats or rabbits, the most intense hæmoglobinuria may be produced without any trace of jaundice (Steiner, Legg, Brunton, Hunter) (16).

And the same rule applies to man. The most intense hæmoglobinuria may occur without a trace of bile pigment in the urine, and without a trace of jaundice (for example, paroxysmal hæmoglobinuria)

It appears to me, then, that the jaundice depends upon some factor other than the mere amount of hæmoglobin set free. The relation between it and the blood-destruction is, in my opinion, no simple quantitative one as Kuhne assumed. The jaundice may be absent even when the hæmoglobinæmia (with hæmoglobinuria) is intense; as in paroxysmal hæmoglobinuria, or in blood-destruction by injection of distilled water. It may be extreme when there is no hæmoglobinuria, as in icterus gravis, Weil's disease, or toluylendiamin poisoning in dogs.

Nor is the jaundice simply related to the increase of bile pigments *due to the preceding blood-destruction—simply a "jaundice from polychromia," as Stadelmann has suggested. For here again I would point* out that the relation is not constant. Jaundice may be slight or absent when the increase of bile pigments is very great, as in poisoning with arseniuretted hydrogen, or in pernicious anæmia; or, on the other hand, it may be extreme when the increase is only relatively moderate, as in toluylendiamin poisoning.

Thus, neither as regards amount of hæmoglobin liberated, nor as regards bile pigments formed, is the relation a mere quantitative one. The relation is clearly rather of a qualitative than of a quantitative character.

Different agents present certain differences in their mode of action on the blood, to which importance has been attached by certain observers in this relation (Afanassiew, Silbermann). Some, such as glycerine or distilled water, cause intense hæmoglobinuria, leaving but a small proportion of hæmoglobin to be dealt with by the liver and other organs. Others appear rather to break up the red corpuscles into fragments which accumulate in the liver (and other organs), a portion only escaping through the kidneys; and the increased excretion of bile thereby occasioned is liable to be attended with jaundice. To this class belongs the chief jaundice-producing agent—toluylendiamin. A third group, like pyrogallic acid, are intermediate in their action, causing both hæmoglobinuria and a slight degree of jaundice.

Whatever interest such differences may have, they are, I consider, insufficient of themselves to account for the great difference in the action of the above-mentioned agents in producing jaundice (16). Doubtless they may serve in some degree to explain why one kind of agent causes hæmoglobinuria more than another; but they quite fail to account for the remarkable facts we have already observed —why, for instance, one drug which causes but a limited amount of blood-destruction, without hæmoglobinuria, is capable of producing intense jaundice; while another which causes a much greater blood-destruction, and an intense hæmoglobinuria, fails to produce any jaundice at all.

In addition to the hæmolytic changes in the blood and increase of pigment in the bile just noted, the foregoing observations have revealed another change of more importance than any other in relation to this subject of jaundice. This change is increased viscidity of bile, amounting at the height of the jaundice even to a replacement of it by clear viscid mucus free from bile. To this more than to any other change I find the degree of jaundice related, and the degree of obstruction proportioned. I have shown for the chief of these icterogenetic poisons that this viscidity is due to extensive and widespread catarrh of the bile-ducts set up by the irritant action of the poison (or of its products) in course of its excretion in the bile—an irritant action so great that in certain cases it may excite the most intense duodenitis.

It is not its destructive action on the blood, but the action of the *poison on the liver-cells and epithelium of the bile-ducts during its* excretion, that appears then, so far as our observations go at present, to be the chief determining factor in the occurrence or non-occurrence of jaundice in disorder of the blood. The liability of a poison to produce jaundice is, I consider, proportioned to its irritant action on the liver and epithelium of the bile-ducts in the course of its excretion through the bile, not to its power of causing blood-destruction. And to this variety of catarrh the name "toxæmic" may be conveniently applied, to distinguish it from the ordinary form of catarrhal jaundice of "duodenal" origin, from which it is essentially distinct. The term "toxæmic" indicates the blood origin of the condition; that it is produced by excretion of poisons from the blood through the bile. It also indicates the chief character of the clinical features of these cases of jaundice, which are mainly of a toxic character.

D. Jaundice by suppression; "Ictère hémapheique," "Urobilin icterus."—In the class of cases hitherto considered it has been assumed that the jaundice has been always marked by the presence of bile pigment in the urine. There is a class of cases, however, to which reference must now be made where this is not the case; where, with a discoloration of skin hardly distinguishable from that of jaundice and a high colour of the urine resembling that of jaundiced urine, the pigments in the urine are not bile pigment, but other pigment derivatives of hæmoglobin of a more or less obscure nature. The coloration of skin in these cases is usually not so deep as that found in ordinary obstructive jaundice; and it is of a more dirty earthy tint.

This kind of jaundice has received various names at different times. It constitutes one of the many forms of "jaundice by suppression" of older writers; it was named by Gubler (1857), and French writers following him, "l'ictère hémapheique", it is the "urobilin icterus" of more recent writers, chiefly German. These names are by no means equivalent, but they are conveniently considered together, because all three imply that the cause of the discoloration is the presence of pigments circulating in the blood as the result of some faulty excretion, or even of entire suppression of function of the hepatic cell.

Of all the various opinions regarding the mode of origin of jaundice, that of a *jaundice by suppression* is both the oldest and the one most firmly rooted. We have seen that the class of cases referable to this category has been very greatly narrowed by recent observations. But even when all the cases arising in connection with the action of poisons and with increased blood-destruction are excluded, as now they must be, there still remain the few cases that suffice to raise the questions: "What is to be understood by suppression of liver function? Does it occur? If it does, what part does it play in producing jaundice?" In other words, is it possible for the liver-cell, without undergoing structural change, to cease to act altogether, to "strike work" (Harley)?

I have said "without structural change"; for this is the only point on which any difference of opinion can reasonably exist. It is obvious that a liver-cell structurally disorganised, as is the case in the later stages of many liver diseases—notably in acute yellow atrophy—must fail in its functional power. Moreover, there can be no doubt that many of the *poisons capable of inducing jaundice affect the liver-cells injuriously, both in their structure—causing fatty parenchymatous degeneration—and, presumably, in their function also* Indeed the latter may be said to have been shown beyond doubt; for it has been found, experimentally, that under the influence of poisons or other depressant factors, such as injury of the liver, hæmoglobin may pass through the liver-cell unchanged, and be found free in the bile; an occurrence which never takes place otherwise. These facts may be admitted. But the theory of suppression implies something more than mere functional disorder; it implies that, as the result of certain influences—nervous as well as toxic—the liver-cell can dynamically be suddenly thrown out of action without any necessary static change, and that the effect of this arrest of function is to dam up within the blood the bile pigment which would otherwise have been duly excreted.

It is this doctrine which meets us at every point when we consider the pathology of jaundice, and which therefore must be considered in more detail. In a more or less modified form it is still held to apply to the jaundice of mental emotion, and indeed to some of the forms of jaundice produced by poisons; but the facts on which it is based are for the most part exceedingly indefinite. So long as the view was held that the bile pigments are formed in the blood, their mere retention in the blood and tissues and appearance in the urine, especially when unaccompanied by any bile acids, were deemed sufficient to point to suppression of liver function. But, as I have shown, such a view is no longer tenable. Bile pigment is not formed within the blood, but within the liver-cell; and its presence in the urine, even when unaccompanied by bile acids, is quite compatible with excessive activity of the liver-cells.

There remain three classes of facts which may be held to denote some interference with the functions of the liver in certain cases of jaundice (*a*) Presence of pigments other than bile pigment in the urine in these cases; (*b*) Changes in nitrogenous metabolism met with in the severest forms of jaundice, for instance, diminished excretion of urea and the appearance of leucin and tyrosin in the urine; (*c*) Presence of colourless mucus in the biliary passages, and absence of bile (Moxon).

(*a*) *Evidence of suppression derived from a study of pigments other than bile pigment.*—In many severe cases of jaundice the urine presents a depth of colour far in excess of what can be accounted for by the quantity of bile pigment present, and obviously denoting the presence of abnormal pigments.

Gubler was led by observation of this fact to distinguish two forms of jaundice: *l'ictère biliphéique*, due to the presence of bile pigment in the tissues; and *l'ictère hémaphéique*, due to the presence of a hypothetical pigment, "hemaphein." He considered that if the liver were thrown out of ction by poisons or other influences it could no longer transform hæmoglobin into bile pigment; the colouring matters in the blood would accumulate there, and undergo various modifications before their excretion in the urine.

Various organic diseases of the liver, such as cirrhosis and cancer, could bring about a similar suppression. Indeed cases of ordinary obstructive jaundice, if unduly prolonged or intense in degree, would lead to the same result.

This view of Gubler has now only a historical interest, inasmuch as the pigment he termed *hemaphein* had never more than a hypothetical existence. So far as it conforms in its characters to any definite urinary pigment, it approximates most closely, as Quincke has shown, to the pigment urobilin. And since Gubler's time, more especially of late years, the class of case to which his view referred has been most frequently discussed under the title of "urobilin jaundice."

"Urobilin Jaundice."—It is chiefly to this pigment urobilin, and another urinary pigment urohæmatoporphyrin, that most of our knowledge of the urinary pigments relates. First recognised as a normal pigment of the urine by Jaffé in 1863, urobilin was soon afterwards (1871) shown by Maly to be identical with one obtainable by reduction from bilirubin, the chief bile pigment, and, subsequently (1874), Hoppe-Seyler succeeded in preparing it artificially from hæmatin.

The later studies of MacMunn (1889), and the still more recent and exhaustive studies, carried out on greatly improved methods, of Garrod and Hopkins (1896), have added greatly to our knowledge of its characters, and its affinities to the pigments of the bile. In particular, since the important observation made by Muller (1892) that intestinal micro-organisms possess the power of transforming bilirubin into urobilin, evidence has steadily accumulated that this is probably the ordinary mode of origin of urobilin; although the possibility of a direct conversion of hæmoglobin into urobilin under certain special circumstances cannot be altogether excluded.

Urobilin is a normal constituent of the urine, and especially abundant in febrile urines; but the conditions under which it is met with in excess are those in which large extravasations of blood are being absorbed (hæmatoceles), or an abnormal destruction of blood is occurring (pernicious anæmia); conditions I have elsewhere shortly defined as "an excessive destruction of hæmoglobin unattended by hæmoglobinuria."

Its presence under such circumstances has a special interest in relation to our present subject, as it is not infrequently associated with a certain yellowish, apparently icteric tinge of skin and conjunctiva. It is this association that has led some observers to apply to the condition the title *urobilin jaundice.*

The precise conditions which determine the amount of urobilin in the urine in cases of jaundice are as yet but ill defined. Hardly any two observers are agreed upon them. While according to Hoppe-Seyler an increased excretion of urobilin is found at the very outset in obstructive jaundice, according to another author (Kunkel) it is most abundant towards the end, being then derived from the bilirubin in the tissues; and yet a third (Hayem and Quincke) find that obstructive jaundice may run its entire course with only a trace of urobilin in the urine.

The following are Quincke's conclusions with regard to the relationship of urobilinuria and jaundice:—

(i.) If much bile pigment be present in the blood a part is deposited in the tissues, a second part is excreted unchanged in the urine, and a third is excreted as urobilin.

(ii.) If less bile pigment be present in the blood, less is deposited in the tissues, the whole or the greater part being converted into urobilin.

The group of cases of severe jaundice in which there is abundance of bile pigment in the urine, and only a trace of urobilin, cannot be accounted for on any view which implies that urobilin is formed from bilirubin within the tissues. But in the light of the more recent observations referred to, establishing the intestinal origin of urobilin from bilirubin by the action of micro-organisms, this class of cases becomes clear. For in severe jaundice, with no bile entering the intestine, we might expect the formation of urobilin to be lessened or even to cease.

Conversely the conditions in which urobilin might be expected in excess are those in which, along with some degree of jaundice, there is also an increased secretion of bile pigments; and it is precisely in such conditions—those of *hæmo-hepatogenous jaundice* already considered—that, as a matter of experience, urobilin is usually found in excess.

Whatever be the precise conditions which determine the amount of urobilin in the urine, and these are probably chiefly intestinal, the important point is that the title *urobilin jaundice* is, under any circumstances, a misnomer. The staining power of urobilin is very small compared with that of bilirubin; and it is not its presence, in however large an amount, that produces the jaundice with which it is sometimes associated, but the presence of bile pigment. Thus urobilin may be present in the urine in the greatest excess without any trace of jaundice, albeit the skin may have a lemonish yellow hue which at first sight resembles jaundice. This is best observed in cases of pernicious anæmia. I have described a severe case of this kind, lasting for months, unaccompanied by any trace of bile pigment in the urine, the urobilin in which was so abundant that its band could be easily recognised after sevenfold dilution of the urine; its amount varying from time to time with the periodic exacerbations of the hæmolytic process.

I find myself thus in entire agreement with Quincke, Stadelmann, and Chauffard as to the non-existence of a jaundice due to urobilin. And I find no evidence that any other pigment possesses any greater power in this respect than urobilin, though no doubt other pigments, modifications of those of health, are present in such cases.

For the group of cases of so-called suppression jaundice, where the suppression is ascribed to nervous influences, I find no evidence whatever that the pigments excreted differ in any way from those of ordinary obstructive jaundice; or that there is any "suppression" of excretory function on the part of the liver.

In severe toxæmic conditions—such as characterise the gravest forms of jaundice, malignant jaundice, acute yellow atrophy, and the like—where the liver is extensively disorganised, and the excretion through the kidneys is interfered with owing to degenerative changes in the cells of the tubules, it is probable that abnormal pigments may be formed, and may give a special character to the coexistent jaundice. We know that in septic conditions of the blood—and in all severe cases of jaundice hæmorrhages are almost a constant feature—the hæmoglobin is more unstable than in health. Thus, as Dr. Copeman has shown, if a drop of putrid serum be added to healthy blood under a cover-glass, crystals of reduced hæmoglobin appear in from 24 to 48 hours; whereas normal blood alone undergoes no crystallisation. On the other hand, in certain toxic conditions — for example, cancrum oris, septicæmia, erysipelas, pernicious anæmia—the blood readily crystallises without addition of any putrid serum. It is very probable that, in severe forms of blood disorder marked by jaundice, abnormal pigment derivatives of hæmoglobin may be formed and be excreted in the urine. But their presence under such circumstances does not necessarily indicate a suppression of the excretory function of the liver, as the suppression theory of jaundice implies. It is sufficiently accounted for by disordered function of the liver consequent on the toxic condition of the blood. For functional disorder is a condition wholly distinct from total suppression of excretory function.

Thus a liver-cell, under the influence of a severe poison, may have its functions so affected that, instead of breaking up hæmoglobin into normal bile pigment, it produces abnormal bile pigments: such I consider quite a permissible assumption; and this of itself is sufficient to account for the presence of abnormal pigments. But that under the influence of mental emotion, or the action of a severe poison, the whole of the liver, without undergoing previous structural change, may cease to work, and that the effect of such a suppression is to produce jaundice, damming up bile pigment or allied pigments, finds, in my opinion, no support whatever from any facts concerning the character of the pigment, urinary or other, excreted in such cases.

(*b*) *Evidence of suppression derived from a study of changes in metabolism.*—The second class of facts adduced as evidence of suppression of liver function in jaundice is the occurrence of marked changes in the nitrogenous metabolism in severe cases of jaundice—for example, diminished excretion of urea; appearance of leucin and tyrosin in the urine.

Thus with regard to the jaundice produced by phosphorus—always cited as an eminent example of a jaundice from suppression—in the first observations made (Schultzen and Riess, 1870), the urea appeared to be reduced almost to vanishing-point, and its place to be taken by other products, lactic acid especially being very abundant. That such changes should occur in the later stages when the liver-cells have become structurally disorganised, is easy to understand. But the question here at issue is to what extent the metabolic functions of the liver are suppressed at the outset when jaundice first makes its appearance.

It is in connection with the jaundice of phosphorus poisoning that the most exact and detailed observations bearing on this point have been made within recent years; namely, those of Münzer (1894). This observer has estimated the total excretion of nitrogen in ten cases of phosphorus poisoning, determining at the same time the proportions of urea, uric acid, ammonia, and extractives of which the total was made up [*vide* p. 89]. Münzer's observations bring out the remarkable fact that, so far from the excretion of urea being diminished, after the first twenty-four hours when the vomiting has ceased, the excretion continues up almost to a few hours of death, in quantities approaching those of health, and far exceeding what would be formed by a healthy liver in the absence of food. Since all recent observations agree in pointing to the liver as the chief seat of urea-formation, this excretion is such as to denote that a very active metabolism is going on within the liver up to within a few hours of death.

This conclusion is brought out still more clearly by some further facts.

As an indication of the degree of liver activity, even more important than the actual amount of urea formed, is the proportion of urea to the total nitrogenous excretion. The experiments of Schroeder have established satisfactorily that the liver is the chief seat of the formation of urea, and that it is formed there by a process of synthesis from ammonia.

In health *urea* constitutes about 85 to 90 per cent of the total nitrogenous excretion, *ammonia* from 4 to 6 per cent, the remainder being in the form of *extractives.*

If the liver be cut off from the circulation there is a marked fall in the proportion as well as in the amount of urea, and a corresponding rise in the proportion of ammonia.

Now, what is found in phosphorus poisoning is, that the proportion of urea is but little reduced (80 instead of 90 per cent), the corresponding increase of ammonia being moderate (10 to 18 per cent instead of the normal 4 to 6 per cent). This alteration, slight though it be, might be held to indicate that the functional activity of the liver is affected—is "suppressed" to that extent; but even this significance cannot be attached to it. Apart altogether from activity of the liver, there is one condition which more than any other influences the amount of ammonia excreted, namely, the degree of alkalinity of the blood. Anything that tends to lower the alkalinity of the blood below the normal standard tends to raise the proportion of ammonia excreted in the urine at the expense of the urea. Now such a tendency exists in phosphorus poisoning. An increased acidity of the blood (as well as of the urine) has been shown by von Jaksch to be a feature of phosphorus poisoning. And not Munzer only, but Starling and Hopkins also, who, before Munzer, had observed this slight increase in the proportion of ammonia in a case of phosphorus poisoning, are agreed in their opinion that the increase is to be referred to this change in the blood rather than to any impaired activity of the liver. *Experiments conducted by Munzer to test the question appear,* indeed, to be conclusive on this point.

To sum up, then, with regard to the jaundice of phosphorus poisoning, the facts show that at the time at which the jaundice makes its appearance the liver functions are by no means suppressed. On the contrary, whether we have regard to the bile-forming functions, or the functions concerned with nitrogenous metabolism, the activity of the liver is hardly diminished. For not only is there an increased formation and excretion of bile pigments (Stadelmann), but, notwithstanding the absence of food, urea also continues to be formed in large quantity up to the last few hours of life, in amounts approximating those of health (Munzer).

(*c*) *Absence of bile from bile passages as an evidence of suppression.*—The fact that in certain cases of jaundice the bile passages are found filled with an almost colourless mucus, instead of bile, has been much insisted on by Moxon and others as an evidence of suppression of excretory function on the part of the liver. But as pointed out, in my opinion correctly, by Dr. Wickham Legg, the presence of such mucus in the large bile-ducts is only evidence that the obstruction is higher up in the smaller ducts. "These continue to receive the bile poured into them by the lower cells, but the bile does not reach the large ducts because the smaller are shut off from the large either by plugs of tenacious mucus or by gravel." Although the larger ducts are colourless, the smaller ducts can be found stained with bile. Stadelmann's experiments show that in the jaundice produced by poisons the bile becomes viscid and mucoid at the time the jaundice is most intense. Examination of the liver itself at this time shows the smaller bile-ducts and capillaries to be filled with thick, viscid, highly pigmented bile.

Conclusion.—Neither the facts concerning the pigments nor those concerning nitrogenous metabolism appear to lend any support to the hypothesis of jaundice by suppression without structural change. There is no conclusive evidence that a healthy liver can be suddenly thrown out of action, whether by nervous action or the action of a poison; or that jaundice can thus be caused. There is evidence on the contrary that a liver so obviously diseased as the liver in phosphorus poisoning is, continues to discharge some of its most important functions almost unimpaired within a few hours of death.

Nor is my judgment as to this hypothesis affected by the modification of it recently put forward by Liebermeister (1893). Liebermeister, one of the oldest of observers on the subject of liver disease, considers that in certain cases, under the influence of mental emotion or action of poisons, there may be suppression of only one particular function of the liver-cell. Apart from forming the bile pigments, he considers one of the chief functions of the liver-cell to be that, notwithstanding its close relation to blood capillaries and lymphatics, it excretes its bile into the bile capillaries, and prevents it from entering the blood. For the dis-

charge of this function the integrity of the cell is necessary. It is not to be assumed that cells profoundly affected by nerve influence or poison, as the case may be, will discharge this function properly. It is rather to be supposed that under such circumstances they will no longer be able to prevent direct diffusion of their contents into the blood and lymph, just as in renal disease the living endothelium of the vessels can no longer retain albumin. Apart, therefore, from any obstruction, jaundice, he says, might thus arise; and all the more readily inasmuch as it is precisely in such cases that degenerative changes are found in the whole or in a large number of the liver-cells. He goes even farther, and conceives that the cell might be only partially affected in its functions, still being able to produce bile although no longer able to prevent its diffusion into the blood; or that the cells in one portion of the liver might continue to produce bile, which afterwards comes into relation with others that had lost their power of retention. Jaundice so caused, by failure on the part of the liver-cell to retain its bile, he proposes to designate "akathektic" jaundice (*kathektikos* = retentive). This view is one capable neither of proof nor disproof; one which, under any circumstances, could only be entertained when all other explanations fail.

E. Increased secretion, with excessive absorption of bile from the intestine, as a cause of jaundice; "Jaundice from polycholia."—The cases so described correspond for the most part with those designated hæmatogenous. Of the latter, indeed, a polycholia was deemed to be a distinguishing feature; if the stools were free from bile, the jaundice was of obstructive origin; if they contained bile, its origin was hæmatogenous.

We now know, in the light of Stadelmann's observations, that the jaundice in these latter cases is no less obstructive than in the former; and that the cause of it is not the increase of bile (polycholia) itself, but the increased viscidity of bile which usually accompanies the polycholia. Indeed exception is taken by Stadelmann to the use of the term "polycholia" at all in this relation; inasmuch as both its watery constituents and its bile acids are usually diminished. It is really a "polychromia," an increase of bile pigments.

Even when this large group of cases are excluded, as now they must be, from the category of jaundice from polycholia, we have still to inquire whether, as Frerichs taught, jaundice can result from increased absorption of bile from the intestine.

This teaching received the support of Murchison. He considered it to be the explanation of jaundice in congestion of the liver; in many cases of which, as he pointed out, the quantity of bile is increased. "The vessels of the liver are distended, and the diffusing surface of the walls is consequently increased, and more than the normal quantity of bile is taken up into the blood. . . . There is no obstruction of the bile-ducts unless there be concurrent inflammation of the duodenum and ducts; and sometimes indeed there is bilious diarrhœa. If the bowels be constipated, the jaundice from congestion of the liver will probably be *increased, as the bile instead of being cleared away will accumulate in the* biliary passage, and will be absorbed in all the larger quantity by the distended vessels. A sluggish state of the bowels often contributes to the development of jaundice, partly by impeding the portal circulation and inducing congestion of the liver, partly by causing an accumulation of bile in the biliary passages and duodenum, and thus favouring its absorption into the blood."

It is clear from the foregoing that although Murchison had chiefly in view an increased absorption from the bile passages, not directly from the intestine, he had also in view in such cases a direct absorption of bile into the blood-vessels of the liver from increase of their diffusing surface. In the light of more recent observations, it must, I think, be regarded as exceedingly doubtful whether such a direct absorption ever takes place. Saunders was the first to show (1815) that, after ligature of the bile-duct, the chief absorption of bile takes place through the lymphatics. Later Fleischl (1874), working under Ludwig, showed that if after such ligature care be taken to prevent any lymph entering the general circulation (by tying a canula in the thoracic duct and collecting the lymph externally) no jaundice results. Under these circumstances no absorption whatever occurs directly into the blood.

More recently (1892) these experiments have been repeated and strikingly confirmed by Vaughan Harley, also working under Ludwig. He found that under these circumstances not only does no immediate jaundice occur, but also that jaundice remains absent for as long as seventeen to twenty days later.

When it is remembered how close are the relations of bile capillaries and blood capillaries, separated as they are only by the thickness of the liver-cell interposed, the above results are very striking. That under these favourable circumstances bile is not reabsorbed by the liver-cells and does not enter the blood directly, but continues to be excreted into the bile capillaries and thence absorbed by the lymphatics, affords convincing proof that absorption of bile is not a matter of extent of diffusing surface between bile and blood capillaries respectively. Bile once excreted is absorbed only by lymphatics, not by the blood-vessels directly.

As regards congestion of the liver in particular, it is, I think, unnecessary to call in the aid of any unusual factor to explain its jaundice. That is sufficiently accounted for by the prevailing condition of congestion and catarrh, which favours temporary stagnation of bile in the bile passages with or without increased secretion of bile

The view of a jaundice from polycholia implies, however, more than a mere absorption of bile within the liver, whether through lymphatics or blood-vessels. It implies that such an absorption may take place from the intestine; that the absorption which normally takes place may become so increased that the liver is no longer able to dispose of all the bile pigment conveyed to it, and that some of it escapes into the general circulation and produces jaundice. This view assumes, first, that bile out normally absorbed from the intestine into the portal blood; secondly, that *this absorption may be so great that the liver cannot excrete all the pigment conveyed to it; that is, there is a relative incompetence of the liver.*

The basis for this view is the hypothesis of "the circulation of the bile" put forward by Schiff (1868). He observed that in dogs with biliary fistula the secretion of bile diminished when the bile was withheld from the intestine; whereas it immediately became increased if the bile were allowed to flow again into the intestine. The same thing was observed if, instead of bile, bile salts were injected into the duodenum. He concluded that the increase arose from absorption of bile into the portal blood again to be excreted by the liver; that what might be termed a "circulation of bile" thus took place within the portal system.

Similar observations were made by Rutherford and Vignal in their experiments (1876): injection of bile into the intestine was followed by increased flow of bile. Together they afford at least presumptive evidence that a portion of the increase is actually due to the absorption and excretion of the injected bile. But although later observations conclusively show (Tarchanoff, Wertheimer) that bile pigment injected into the blood is without doubt excreted in part in the bile, the evidence that increased absorption of bile from the intestine plays any part in producing jaundice remains still little more than presumptive.

That the liver exercises an important excretory and destructive function in respect of certain substances normally absorbed from the intestine in the portal blood is beyond dispute. Interference with this function, with the passage of such products into the general circulation, is probably accountable for some of the more characteristic symptoms of liver disorder—intense depression of spirits, drowsiness, sense of giddiness, headache, pains on moving the eyeballs. And it may be regarded as equally beyond dispute that whatever bile pigment is absorbed in the portal blood is again excreted in the bile.

But what, in my opinion, is much open to question is the extent to which such an absorption occurs in health, and whether it is ever a factor in producing jaundice. Wertheimer's observations, striking as they are, I cannot regard as conclusive on the point. The bile of the sheep contains a pigment, with definite spectroscopic bands, not present in the bile of the dog. After injection of sheep's bile into the circulation of the dog Wertheimer was able to discover the pigment in the dog's bile.

Were jaundice produced in this way it would appear not only in the one condition adduced by Murchison of congestion of the liver, but in other conditions also where the increase of bile is even more marked; namely, under the action of hæmolytic poisons generally. But in all these cases, where a polycholia exists, the conditions favouring an absorption of bile into the circulation are created before the bile reaches the intestine, namely, within the liver itself and its bile-ducts, and have been brought about by increased viscidity of bile. The jaundice is thus not of intestinal but of hepatogenous origin.

F. The influence of the nervous system in producing jaundice.—The nervous system has long been credited with a very direct influence in the production of certain forms of jaundice.

According to some authors, indeed, disturbance of the nervous system plays a part of considerable importance in nearly all forms of jaundice, from the simplest "bilious attack" to the gravest form of all, namely, acute yellow atrophy of liver. The former malady has been regarded as an evidence of altered nerve function (Habershon); and in the latter, deranged innervation has been considered to play a chief part (Liebermeister), either by causing perverted secretion in which the liver-cells become broken up (Rokitansky), or by causing paralysis of the bile-ducts (von Dusch). In a considerable proportion of cases (one-tenth, Thierfelder) the only cause assignable for the disease has been the influence of fright, or some depressing mental emotion.

Apart, however, from these cases, where the influence of the nervous system in causing the jaundice is, I consider, more or less purely speculative, the cases regarded as manifesting this influence more clearly are those in which jaundice has followed sudden or severe mental emotion or strain—such as fear, anger, or anxiety—either immediately or very soon after. Of this character, also, is supposed to be the jaundice following on concussion of the brain.

The cases may be divided into two classes—

(i.) In the one—an extremely small class—the jaundice is described as following immediately, that is, in a far shorter time than ordinary obstruction could produce it Of this nature are the two cases of Villeneuve (1818) quoted by Murchison. A soldier, insulted in public, in a fit of furious anger became suddenly jaundiced, soon afterwards delirious, and died in convulsions A priest had a sudden fright from the rush of a mad dog; he uttered a loud cry, fell down unconscious, and was taken up yellow as saffron.

(ii.) The other class of case—comparatively common—is where the jaundice occurs in the course of a few hours after anxiety or great mental strain. Of this nature is the case of the youth quoted by Sir Thomas Watson, who had an attack of intense jaundice apparently traceable to nothing but overdue anxiety about an approaching examination; or that of the doctor who, while attending a case of puerperal hæmorrhage, became deeply jaundiced in one night.

The mechanism of the jaundice in such cases is by no means clear And the features that appear to suggest nervous derangement as distinguished from obstruction, especially in cases of the first class, are, first, the suddenness of onset of the jaundice—the skin becoming yellow almost in an instant, whereas the jaundice from mechanical obstruction takes twelve to twenty-four hours or more to develop; and, secondly, the frequency with which such cases are said to be marked by cerebral symptoms—delirium, coma, convulsions.

(i.) Cases of instantaneous jaundice are admitted to be of great rarity. Most of them date from the earlier history of the subject. But assuming such cases to occur, they raise points of interest as to the possible part taken by the nervous system in producing jaundice.

Various views have been put forward:—

(*a*) Like every other variety of obscure jaundice, it has been referred to *suppression* of liver function. Under the influence of powerful emotion the function of the liver-cell becomes temporarily arrested, and jaundice results. We have seen, however, that there is no theory of jaundice so unsatisfactory as this of suppression. If the jaundice in these cases were shown to be produced by pigments other than bile pigments, there might be ground for assuming such a suppression; but this is not so. The jaundice is due to the presence of bile pigments, formed as we have seen by the liver-cell; and the problem is to account for their passage into the blood: whether they pass into the blood capillaries directly or indirectly in the usual way through the lymphatics.

The suddenness of onset would appear to point to direct absorption; and it has been suggested (Brunton) that this might be brought about by some sudden fall of blood-pressure within the portal system, such as emotion might cause, followed by a sudden absorption of bile from the bile capillaries.

(*b*) This view raises the question of the *relation of the blood-pressure to bile secretion* under normal circumstances. The conditions within the liver are so far peculiar, that it is from the venous blood-supply—the portal blood, not the arterial—that the liver obtains the chief material for its metabolism, including the formation of bile. The chief function of the hepatic artery is to supply the tissue framework of the liver. The main supply is through the portal system. It follows from this arrangement that, to an extent quite unusual in the case of any other organ, the supply of blood to the liver and its functional activity are independent of any direct vaso-motor control. It is regulated rather in an indirect manner by the amount of blood entering the portal system through the intestine. Variations in the general blood pressure affect it little. Thus Heidenhain found that a fall in the general pressure even so great as one-half appeared to influence the secretion of bile but little. On the other hand, variations in the portal pressure do affect it materially. Thus stimulation of the spinal cord, or of the sensory nerves, by causing contraction of the splanchnic vessels and thus diminishing the amount of blood entering the portal system, occasions a diminished secretion of bile. And, conversely, section of the splanchnic nerves, by causing a dilatation of blood-vessels in the portal area, and thus increasing the flow of blood through them, occasions an increased secretion of bile.

The secretion and flow of bile being thus chiefly influenced by the flow of blood within the portal system, the question arises whether sudden and extreme variations in the direction of a fall of pressure can affect the flow of bile to such an extent as to arrest it altogether, and cause its direct absorption into the blood. Now even in health the pressure within the portal system is very low and, what is still more important, is much lower (nearly two and a half times) than that at which the bile is secreted. The conditions might thus appear to be permanently favourable to a direct absorption of bile into the blood-vessels. And yet, as we have seen, so far is this from taking place that even after ligature of the bile-duct the bile cannot be made to pass into the blood-vessels. It is absorbed through the lymphatics. Whether, under the influence of emotion or other powerful nervous shock, these conditions can be altered, appears to me to be exceedingly doubtful.

(*c*) To account for the sudden onset of the jaundice in such cases another possible factor may be suggested as the result of sudden emotion, namely, *spasm of the bile-ducts*, at a time when the secretion and flow of bile are in active progress.

Peristalsis of the walls of the bile-ducts and gall-bladder must, I consider, play a more prominent part in the actual propulsion of bile into the duodenum than is generally supposed.

The effect of sudden emotion on the peristaltic movements of the intestine is well known. And it is conceivable that in rare cases—and, after all, the cases now under consideration are of extreme rarity—under the favouring conditions above described, sudden mental emotion of the nature of fear and anger might occasion a spasm of the bile-ducts of the nature here contemplated. Assuming that such cases occur, it is in this direction, rather than in that of suppression, or direct absorption into the blood-stream, that, as it appears to me, the most likely explanation of the jaundice is to be found.

(ii.) The more common class of cases referred to nervous derangement—those, namely, where the jaundice appears more gradually, albeit still quickly—say in the course of twelve or twenty-four hours or more—present less difficulty, and can be accounted for without calling in the aid of such special factors. The effect of grief and anxiety in arresting digestion, and in producing acute indigestion with all the symptoms of gastric and duodenal catarrh, need not be dwelt on. In the case of a medical man under my observation it led in the course of one night to a condition just short of actual jaundice; the stools were clay-coloured, there was great distress in the region of pit of stomach and duodenum, and the complexion was distinctly sallow; but by urgent measures the actual onset of jaundice was prevented.

In these cases the jaundice is doubtless of catarrhal origin—more sudden in onset than usual, it is true, but pursuing subsequently the same course and disappearing in about eight days.

SUMMARY OF THE VARIOUS FACTORS.—As possible factors, other than mechanical obstruction, in the causation of jaundice we have had to consider:—

1. Hæmatogenous origin of bile pigment ("Hæmatogenous Jaundice"). We have seen that the normal seat of formation of bile pigment is within the liver-cell. A hæmatogenous origin of bile pigment sufficient in degree to cause jaundice does not occur.

2. Suppression of function ("Jaundice by Suppression").

(*a*) Suppression of Biliary Function. Pigments other than bile pigment as a cause of jaundice ("L'ictère hémapheique," "Urobilin Jaundice").

There is no conclusive evidence of any such causation of jaundice. Pigments other than bile pigment may be formed, and may in certain cases produce some discoloration; but this is totally distinct from jaundice.

In many cases of jaundice evidence of altered activity of liver-cells is forthcoming; for example, diminished secretion of bile, increased formation of bile pigments, diminished formation of bile acids: but such changes cannot be regarded as indicating "suppression" of biliary function. On the contrary, in the larger number of such cases the most marked feature is an increased formation of bile pigments—evidence, therefore, of increased activity rather than of suppression of function.

(*b*) Suppression of Metabolic Function. Diminished formation of urea, appearance of leucin and tyrosin in urine.

Besides the formation of bile, the formation of urea may be taken as an index of liver activity; all evidence going to show that urea is formed by process of synthesis from ammonia, and that the synthesis takes place within the liver-cell.

In health urea constitutes about 85-90 per cent of the total nitrogenous excretion of the urine, the remainder being made up of ammonia and extractives.

In jaundice, even in the severest cases such as phosphorus poisoning, this proportion may remain unchanged, or at most slightly lowered, so that at the time the jaundice appears, no evidence is forthcoming of any "suppression" of liver function, as regards urea-formation, in the sense assumed by the "suppression theory" of jaundice; namely, suppression of function apart from structural alteration.

It is thus extremely doubtful whether total "suppression" of function ever occurs apart from actual destruction of the liver-cell. Hence it is only in the last stages of the severest forms of toxic jaundice—such as acute yellow atrophy of the liver—that the functions of the liver can rightly be said to be "suppressed."

3. Increased secretion of bile with excessive absorption from the intestine ("Jaundice of Polycholia").

Many cases of jaundice, those produced by poisons generally, are marked at one stage or other by increased flow of bile and increased excretion of bile pigment. There is no conclusive evidence that jaundice may result from increased absorption of this bile from the intestine. The jaundice met with under such circumstances is the result of absorption of bile from the bile-ducts.

4. Deranged innervation ("Jaundice of Emotion").

Deranged innervation plays a doubtful, and in any case quite a subordinate part in the production of jaundice.

(*a*) There is no evidence that jaundice can be produced by extreme fall of pressure within the portal system and absorption of bile direct into the blood.

(b) Sudden mental emotion may conceivably cause spasm and reversed peristalsis of the bile-duct, as of involuntary muscle generally.

The two important factors in producing jaundice are:—

5. Increased destruction of blood with increased supply of hæmoglobin to the liver.

6. Action of poisons ("Hæmo-hepatogenous Jaundice").

Both factors are conveniently considered together, as they usually operate together. The most common cause of increased destruction of blood is the action of poisons on the blood. Although operating together these two factors are not of equal importance. *The degree of jaundice is dependent more upon the nature of the poison than the amount of blood-destruction.* The most intense jaundice may be produced by poisons that cause but little or at most a moderate destruction of blood; for example, phosphorus and toluylendiamin. Most of the severe forms of jaundice met with in disease—"Icterus gravis," "Malignant jaundice," "Weil's disease," are of this character, and illustrate this point.

On the other hand, intense destruction of blood may be attended with little or no jaundice: for example, hæmoglobinuria experimentally induced by injection of water, glycerine, or arseniuretted hydrogen; in disease, paroxysmal hæmoglobinuria or pernicious anæmia.

In both cases the jaundice is the result of absorption. It is caused by changes in the liver and in the bile, and is thus in every sense *hepatogenous.* Of most importance are the changes in the bile and smaller bile-ducts. The chief of these are—(a) increased formation of bile pigments (polychromia); (b) diminished formation of bile acids; (c) diminished quantity and increased viscidity of the bile itself. The viscidity retards temporarily the flow of bile along the bile passages; for a time it may arrest it altogether, and is the proximate cause of the absorption. In the case of the most notable jaundice-producing poison—toluylendiamin—this increase of viscidity I have shown to be due to a catarrh of bile-ducts, extending from above downwards (*descending* catarrh), produced by the excretion of the poison through the bile.

Instead, then, of the two varieties of jaundice formerly described, one *hepatogenous* or *obstructive*, the other *hæmatogenous* or *non-obstructive*, it is necessary now to recognise one class only. All jaundice is *hepatogenous*, the result of absorption of bile formed and excreted by the liver. The cause of the absorption may be obvious—mechanical obstruction (*Simple hepatogenous jaundice*), or more obscure and less easily demonstrable swelling and catarrh of the lining epithelium of the bile passages, with consequent increased viscidity of the bile (*Hæmo-hepatogenous jaundice*).

CAUSES OF JAUNDICE

All cases of jaundice may be classed in two great divisions:—

I. Jaundice resulting from obvious mechanical obstruction independent of changes in the blood or bile (Obstructive Jaundice).

II. Jaundice dependent upon changes in the blood and bile; the actual cause of obstruction being increased viscidity of bile, consequent on intrahepatic catarrh (Toxæmic Jaundice).

I. Obstructive Jaundice

The following table of causes is given by Murchison:—

A. *Obstruction by Foreign Bodies within the Duct.*

1. Gall-stones and inspissated bile. 2. Hydatids and distomata. 3. Foreign bodies from the intestines.

B. *Obstruction by Inflammatory Tumefaction of the Duodenum, or of the lining membrane of the Duct with Exudation into its Interior.*

C. *Obstruction by Stricture or Obliteration of the Duct.*

1. Congenital deficiency or obstruction of the duct. 2. Stricture from perihepatitis. 3. Closure of orifice of duct in consequence of an ulcer in the duodenum. 4. Stricture from cicatrisation or ulcers in the bile-ducts. 5. Spasmodic stricture ?

D. *Obstruction by Tumours closing the orifice of the Duct, or growing into its Interior.*

E. *Obstruction by Pressure on the Duct from without by*—

1. Tumour projecting from the liver itself. 2. Enlarged glands in the fissure of the liver. 3. Tumour of the stomach. 4. Tumour of the pancreas. 5. Tumour of the kidney. 6. Post-peritoneal or omental tumour. 7. An abdominal aneurysm. 8. Accumulation of fæces in bowels. 9. A pregnant uterus. 10. Ovarian and uterine tumours.

II. Toxæmic Jaundice

The causes may be divided into three groups—

1. *Definite Poisons*—Toluylendiamin, Phosphorus, Arseniuretted hydrogen.

2. *Poisons formed in various Specific Fevers.*

(*a*) Yellow fever; (*b*) Malaria; (*c*) Enteric fever; (*d*) Relapsing fever; (*e*) Typhus; (*f*) Scarlet fever.

3. *Special Icterogenetic Poisons.*

(*a*) "Epidemic Jaundice." (*b*) "Infectious Jaundice" ("Weil's disease"). (*c*) "Malignant Jaundice." (*d*) "Acute Yellow Atrophy of Liver."

I. OBSTRUCTIVE JAUNDICE

For the symptoms, morbid anatomy, differential diagnosis, and treatment of the several varieties of jaundice caused by mechanical obstruc-

tion, the reader is referred to the various articles dealing fully with the different causes of this condition, as detailed in the foregoing list, namely—

1. Inflammatory affections of gall-bladder and bile-ducts (p. 212). 2. Cholangitis (p. 257). 3. Tumours of the gall-bladder and bile-ducts (p. 226). 4. Gall-stones (p. 234). 5. Tumours of the liver (p. 194). 6. Congenital obliteration of the bile-ducts (p. 249). 7. Cirrhosis of the liver (p. 170). 8. Tumours of the pancreas (p. 272).

II. TOXÆMIC JAUNDICE

SYNONYMS.—*Hæmo-hepatogenous jaundice* (Afanassiew); *Jaundice of polychromia* (Stadelmann); *Non-obstructive jaundice.*

Definition.—A form of jaundice connected with disorder of the blood, met with in a number of conditions; sometimes as a complication of specific febrile conditions, sometimes as the prominent feature of conditions of obscure, probably infective, nature: it is *characterised* by jaundice of varying severity in association with symptoms of more or less general disturbance; in severe cases by fever, delirium, epistaxis, black vomit, albuminuria, and other symptoms of blood disorder: it is *caused* by the agency of various organic poisons, acting on the blood first and subsequently excreted through the liver, leading to altered character and viscidity of the bile, and in severe cases to degenerative changes in the liver-cells.

Varieties.—The varieties of jaundice falling within the scope of the above definition may be grouped in three classes—

1. Jaundice produced by the action of poisons, such as toluylendiamin, phosphorus, arsenic, snake-bite.

2. Jaundice met with in various specific fevers and conditions, such as yellow fever, malaria (remittent and intermittent), pyæmia, relapsing fever, typhus, enteric fever, scarlatina.

3. Jaundice met with in various conditions of unknown but more or less obscure infective nature, and variously designated as "epidemic," "infectious," "febrile," "malignant" jaundice, "icterus gravis," "Weil's disease," "acute yellow atrophy of liver."

General characters.—Although differing widely from one another in severity and in individual character, there are certain general characters common to all these forms of jaundice which seem to mark them off as a distinct group, conveniently described by the term "toxæmic." In all of them the jaundice appears to be independent of any obstruction to the flow of bile, or at any rate no obvious obstruction can be found in the larger ducts. In all of them the jaundice is associated at one time or other with the presence of more or less bile in the stools, sometimes indeed with an excess of bile (polycholia). In all of them bile acids are not present in such quantity in the urine as in cases of jaundice of purely obstructive nature; they may indeed be absent altogether—a point of difference to which, following Leyden's original teaching, it has been customary to attach a significance altogether out of proportion to its *importance.*

We now know from Stadelmann's studies that in all these respects the jaundice met with in disease agrees in its characters with that produced by drugs like phosphorus or toluylendiamin, so closely indeed as to leave no room for doubt that in disease poisons are also at work. In particular a diminished formation of bile acids appears to be a feature of the action of all such agents—even when causing a largely increased formation of bile pigments; so that their absence from the urine or their presence in diminished quantity in these cases is thus satisfactorily accounted for. And so with regard to the presence of bile in the stools—the action of all these icterogenetic drugs is attended at one stage or other by increased formation of bile pigments and increased flow of bile

Turning from these pathological features to those of a more clinical character, the jaundice met with in the foregoing class of cases presents certain general points of resemblance distinguishing it from the jaundice of purely obstructive origin. In the first place, the jaundice is usually less intense in its character than that met with in obstruction, being frequently evidenced by a slight yellowish or greenish-yellow discoloration of skin and conjunctivæ rather than the deep golden yellow or green colour of obstructive jaundice. It appears to be due, as indeed is the case, to the absorption of some, rather than to the retention of all the bile pigment formed.

But while this is its character in general, it may, on the other hand, be as intense as the jaundice of pure obstruction. Of this nature is the jaundice of toluylendiamin poisoning. In severe cases it is as complete and intense as if a ligature had been applied around the bile-duct; but it is only for the time being, for another feature of the jaundice thus caused is that it is of a more temporary character than that caused by mechanical obstruction. It passes off with the condition of blood and bile on which it depends; that is, in the case of jaundice of drugs, as soon as the action of the poison has exhausted itself.

In the second place, this variety of jaundice is generally associated with more constitutional disturbance than is the case with ordinary obstructive jaundice. In the mildest cases, indeed, disturbance is hardly observable. The mildest forms of catarrhal jaundice, occurring in the course of an epidemic outbreak, and obviously, therefore, the result of some more or less infective influence, may not be distinguishable from cases of ordinary "catarrhal" jaundice of duodenal origin, and may present little constitutional disturbance, if any.

But in general some degree of general disturbance there is; and in the severe cases this is of so pronounced a character—dry tongue, fever, delirium, subsultus, convulsions, epistaxis, black vomit, diminished excretion of urine, and albuminuria,—symptoms of the "typhoid state," —that the jaundice becomes only one symptom of a general condition of severe poisoning. Moreover, although the symptoms vary very greatly in their intensity in different classes of cases, they have the same general character. At first sight it might appear necessary to distinguish between the form of jaundice accompanying definite specific fevers, such as malaria, yellow fever, typhoid fever, and the like, and that met with apparently as an independent affection in "epidemic," "febrile," "infectious," "malignant" jaundice, "Weil's disease," "acute yellow atrophy of liver." And still more might it appear necessary to distinguish in this last group of cases between forms apparently so widely diverse as mild cases of catarrhal (epidemic) jaundice and severe cases of "Weil's disease," "malignant jaundice," and cases of that rarest of all diseases, acute yellow atrophy of the liver. But in reality, both from a clinical and a pathological point of view, they all present certain features in which they resemble each other, and no sharp line of distinction can be drawn betwixt them.

The severest cases of an outbreak of catarrhal (epidemic) jaundice may be marked by so much fever and constitutional disturbance as to be indistinguishable from cases of what is variously called "icterus gravis," "febrile jaundice," "infectious jaundice," "malignant jaundice" Similarly, the condition named "Weil's disease," to which so much attention has been drawn of recent years by German observers, differs in no respect from forms of icterus gravis described long ago by many observers —Graves and others. And lastly, as I shall presently have occasion to show, it is not even possible to draw any clear line of demarcation between the severest forms of icterus gravis, or malignant jaundice, and the acute yellow atrophy of the liver. In mode of onset, character of symptoms, progress of case, and lastly, in character of post-mortem appearances, cases have been observed and recorded as occurring in the course of endemic outbreaks of jaundice which were not to be distinguished from acute yellow atrophy of the liver, even in the minutest particulars supposed to be characteristic of the latter disease; such as atrophy of the liver, diminished excretion of urea, and the discovery of tyrosin and leucin in the urine and liver. So far, indeed, as the last-mentioned points are concerned, identical changes—yellow atrophy of the liver, presence of leucin and tyrosin in the liver and in the urine, diminished excretion of urea—have been found by Frerichs, Murchison, and others in severe cases of jaundice occurring in typhus, enteric, and relapsing fevers.

It thus appears that even in their clinical features all these forms of jaundice have a good deal in common. Their symptoms have a generic likeness, from the initial jaundice, with or without general disturbance, common to all alike, to the marked cerebral and toxic phenomena which characterise the severest cases. The differences in character manifested by the special forms are doubtless due to differences in the character and intensity of the poisons. The differences observable in the action of such agents as phosphorus, arseniuretted hydrogen, toluylendiamin, show that the power of inducing jaundice (icterogenetic power) is possessed by poisons in very varying degree.

But whatever the character of the other symptoms, the icterogenetic power is usually associated with three classes of changes—(*a*) destructive changes in the blood; (*b*) alterations in the quantity and quality of *the bile; (c) changes, functional or parenchymatous, according to the severity of the poisonous action on the liver-cells, and, as the case of* toluylendiamin illustrates, on the bile-ducts, and also on the renal cells.

In disease all these modes of action are manifested in varying degree, especially in severe cases; the degree of blood change being frequently shown by the occurrence of bleedings from nose and stomach (black vomit), and the action on the liver and kidneys by the occurrence of extensive parenchymatous changes in both organs.

Etiology.—As regards their etiology the above class of cases have a good deal in common. Their etiology, except in the first class, where we have to deal with the action of definite poisons, such as phosphorus, is obscure. Age, sex, occupation, habits of life are without any definite influence of themselves, except in so far as they favour the incidence of disease of an infective character. For it is to this latter mode of origin that the preponderance of evidence points, even in the isolated (sporadic) cases. This infective character becomes most manifest when, as not infrequently happens, the jaundice assumes an endemic or even epidemic character, affecting those in the same household or district, or spreading over larger areas. But the resemblance between the severe cases met with under such circumstances and the isolated cases—for example, icterus gravis, Weil's disease—where no definite infection can be proved, suggests very strongly that these latter also have an infective origin.

In a number of such cases, indeed, organisms of varying character have been described as occurring in the liver, and within the last few years much evidence of a similar nature has accumulated. Of the nature of the infection nothing definite is known—whether bacterial or of even lower forms of life (varieties of proteus have been described as the accompaniment of certain severe cases of jaundice). There is hardly any reason, however, to doubt its microbic origin; and it is exceedingly probable that it is of very varying character—that the power of forming poisons, possessing more or less icterogenetic properties, is one possessed by a number of different organisms. But the comparative rarity of forms of infective jaundice indicates that the power is not one incident to the ordinary microbes inhabiting the intestinal tract. Moreover, the comparative rarity with which jaundice of this kind is met with, complicating marked infective conditions of the intestinal tract, speaks to the same effect. Thus jaundice is of very rare occurrence in enteric fever. Murchison only met with it on four occasions; Jenner never met with a case at all.

We may take it then, I think, that in these forms of jaundice we have to do with the action of organisms of specific nature, whether of a bacterial or other kind remains still to be shown; organisms of varying character and virulence; limited in their distribution, or even rare, in this country and in temperate climates, but more widely distributed in tropical climes (for example, the infection of yellow fever and of malarious disease, the remarkably endemic character of outbreaks of jaundice in some parts of Southern Australia).

The seat of infection in most cases is probably the intestinal tract. *Intestinal symptoms—for example, diarrhœa, more or less fœtid in* character—form a prominent feature of a large number of such cases at the outset of the illness. And it is extremely likely that in the largest number of cases the infection remains confined to this tract, and does not spread to the blood; the infection of the blood being limited to the poisons absorbed. It is thus readily conceivable that in fatal cases no organisms would be found in the blood or in the liver; and such cases have been recorded by Dreschfeld and others in acute yellow atrophy.

In other cases, however, the infection passes more directly into the blood itself. Of this kind is the jaundice of pyæmia and of snake-bite.

After this general consideration of the characters and features of this variety of jaundice as a whole, I shall now pass to the consideration of the chief forms comprised within the group.

JAUNDICE OF PHOSPHORUS POISONING.—The jaundice of phosphorus poisoning is the best-known example of a jaundice produced by the action of drugs. It was formerly comparatively common; but since legislative measures have been taken in this country and Germany to enforce the use of the insoluble and non-poisonous form of the drug in the making of lucifer matches, it has become decidedly less frequent. In Austria it is still very common.

The poison is usually taken in the form of an infusion of the heads of lucifer matches, sometimes in the form of those rat poisons which contain phosphorus.

Symptoms.—The symptoms vary considerably, according to the dose of the poison taken and the rapidity of its absorption. But usually two stages may be distinguished: one in which the symptoms are mainly those of irritant poisoning, followed by a second in which more characteristic symptoms of toxic poisoning make their appearance, ushered in with jaundice. The duration of the first stage varies according to the amount of the poison taken. It usually lasts from some two to five days; in exceptional cases it may be as long as fourteen to twenty-one days, and one case is recorded by Dr. West where the characteristic symptoms did not make their appearance for six weeks.

The first symptoms usually begin a few hours after the poison has been taken, and take the form of severe burning pain in epigastrium, with intense nausea and vomiting. The vomiting continues almost incessantly, everything taken being rejected, till in the course of twenty-four hours or so the patient may be in a state of collapse. The respiration is very rapid, the pulse small and weak, the tongue and lips dry and red; thirst is incessant. At this time there is great tenderness over the epigastrium and the region of the liver; but the latter is not perceptibly enlarged.

After a time there is a slight remission in the violence of the symptoms. Then the vomiting returns with renewed severity, but the character of the vomit changes. It now contains blood, dark or chocolate-coloured, and the patient becomes jaundiced; the pain and tenderness over epigastrium and region of the liver continue, and the liver dulness is increased. Moreover, nervous symptoms become prominent—intense headache, sometimes hiccup; drowsiness passing into coma, varied with attacks of delirium and sometimes convulsions; and the patient rapidly sinks, dying either from exhaustion or, more suddenly, from heart failure, within twenty-four or forty-eight hours of the onset of the graver symptoms.

Jaundice is a very characteristic feature. In severe cases it is usually noticeable about the second or third day; in milder cases not till the sixth or seventh day. It shows itself at first as a slight icteric tinge of conjunctiva, but is not fully manifested until the second stage of the disease is entered. Although a characteristic symptom, it is by no means a constant one, nor is it necessarily proportionate to the severity of the poisoning. A considerable number of cases of acute phosphorus poisoning without jaundice have been recorded. Hessler found it in twenty-six only out of forty-eight cases. On the other hand, it was only absent in one out of ten cases recorded by Munzer, and that case was a mild one which ended in recovery. Even when present the jaundice may be slight throughout, although in most cases it is well pronounced. It is marked as usual by the presence of bile pigments in the urine; bile acids are usually present also, although in greatly diminished quantity.

Temperature is usually normal or subnormal throughout. It may be raised in the second stage as much as 100° to 103° F. In rare cases it has risen as high as 107° F. just before death.

Hæmorrhages are a constant feature, but they are not so prominent a feature of the jaundice of phosphorus poisoning as they are of the other forms of severe jaundice; for example, of icterus gravis or acute yellow atrophy of liver. At least this is true of hæmorrhages under the skin. The most frequent form the hæmorrhage takes is that of black vomit—hæmorrhage from the mucous membrane of the stomach. The urine is usually free from blood, although in certain cases blood may be present in quantity. Although thus not so prominent as a clinical feature, the occurrence of hæmorrhage is nevertheless a marked post-mortem feature of the disease.

The Liver.—The region of the liver is exquisitely sensitive to pressure throughout. At first no enlargement of liver dulness is to be made out; but in the second stage the liver can be felt, projecting below the costal margin. In some cases also the spleen is perceptibly enlarged.

The *urine* always shows marked changes. Its *quantity* is usually more or less diminished, sometimes throughout; at other times it may be diminished at first, but afterwards increased, again to fall shortly before death. At no time, however, is there ever any approach to anuria. The quantity varies between 300 c.c. and 2000 c.c.—on an average about 750 c.c. Its specific gravity varies from 1020 to 1037, according to quantity; its reaction is strongly acid, a marked feature. The bile pigments and bile acids are nearly always present—the latter in very diminished quantity. Albumin is frequently present, although not invariably, and usually in small quantity. When present, fatty epithelial cells and fatty *casts* are usually also to be found on microscopic examination. In some cases *blood* is present also. Sugar is an extremely rare constituent; only three cases are on record.

The chief changes presented by the urine relate to its nitrogenous constituents. The first observations made — those of Schultzen and Riess, 1870—appeared to indicate that the urea became reduced almost to vanishing-point, and that its place was taken by other products; lactic acid especially being very abundant. More recent observations have shown that this is far from being the case; that although at first diminished, as compared with the normal, the excretion of urea is relatively much increased, considering that the patient can take no food; so much so as to indicate a largely increased destruction of albuminous material as the result of the action of the poison. This subject has recently received most exhaustive study at the hands of a German observer—Munzer (1894). He has estimated the total nitrogenous excretion in the urine in 10 cases of phosphorus poisoning, and determined at the same time the proportion of urea, ammonia, uric acid, and extractives of which the total was made up.

Total Nitrogen.—His observations show that in the first stage of the poisoning there is an extraordinary diminution in the excretion of nitrogen, the total amount falling as low as 2 to 5 grammes daily, instead of the normal mean of about 15 to 18 grammes. These low figures correspond closely to the excretion of nitrogen in starvation; and they are probably to be regarded as such. For in the first stage of the poisoning the patient is unable to retain anything on his stomach, either fluid or solid.

This great diminution does not, however, last long. While the patient is still unable to retain anything there occurs a remarkable rise, as high as 10 to 17 grammes per day; and at or about this height the nitrogenous excretion remains to the end. Usually when these high figures are reached the patient dies. In some cases, however, recovery has still taken place. So large an increase occurring in spite of the absence of food obviously represents a very largely increased destruction of the albumin of the tissues.

Of this total amount the largest proportion continues throughout to be made up of *urea.* But the proportion varies somewhat according to the stage. In health, urea constitutes from 85 to 90 per cent of the total nitrogen of the urine. In the first stage of the poisoning this proportion is unaltered; urea still forms about 91 per cent of the whole. In the second stage it falls somewhat, namely, 70-80 per cent of the total nitrogen. But the absolute excretion of urea is greatly increased, since in this stage, as we have just seen, the total nitrogen rises so much.

Corresponding to this fall in the proportion of urea there is a rise in the proportion of ammonia and extractives, chiefly of the former. In health, *ammonia* constitutes from 4 to 6 per cent of the total nitrogen of the urine. *In the second stage of phosphorus poisoning the proportion rises considerably, 10 to 18 per cent.*

In health, *extractives* constitute about 4 per cent of the total nitrogen. In phosphorus poisoning they undergo a slight increase, 4 to 9 per cent. The nature of these extractives is unknown—whether amido-acids (leucin and tyrosin) or peptones. *Peptones* are found in the urine in a few cases. They were not present in any of Münzer's cases.

Leucin and tyrosin are sometimes found. In one case Munzer found crystals resembling those of tyrosin in the urine. In one case Fraenkel found tyrosin but no leucin.

Uric acid.—In health about 1 to 2 per cent of the total nitrogen is in the form of uric acid. In the first stage of phosphorus poisoning the proportion of uric acid remains fairly normal (1·6 and 1·4 per cent). In the second stage an absolute increase occurs corresponding to the increase in the total nitrogen; but the proportions remain unaltered (1·16, 1·47, and 1·37 per cent). If the patient live long enough a slight relative increase appears (2·45 per cent). On the whole it may be said that in phosphorus poisoning there is a distinct increase in the excretion of uric acid corresponding to the total increase of nitrogen; but that its proportions are unaltered.

Organic acids.—The organic acids include especially volatile fatty acids and lactic acid.

Fatty acids have been found by von Jaksch in the urine in a number of liver affections; and their appearance was thought by him to stand in some relation to the diminished formation of urea, and thus to mark the severity of the disease. This opinion cannot now be held. Fatty acids were only found in one case out of five in which they were looked for by Munzer; and that was in a patient who recovered. Moreover, the urea, so far from being diminished, was increased.

Lactic acid.—This or some allied acid must be present in most cases. For the urine is extremely acid, notwithstanding that the alkaline value of the ammonia present is more than sufficient, according to Münzer, to neutralise all the acids present. The nature of these acids has not yet been determined.

Inorganic constituents.—*Chlorides* fall to a very low amount, under a gramme daily; and do not rise again until recovery sets in. This great fall is doubtless due to the absence of food.

Phosphoric acid.—The phosphoric acid in the urine has two chief sources within the body—the albumin of the tissues and lecithin—the latter a prominent constituent of certain tissues (red corpuscles, liver, and nervous tissue). In health the albumin of the tissues is its chief source; and hence the amount daily excreted stands in a certain proportion to the total nitrogenous excretion, namely, as 18 : 100. This proportion rises whenever there is any increased destruction of lecithin. In phosphorus poisoning there is a distinct absolute increase in the excretion of phosphoric acid during the first two or three days. But still more marked is the relative increase lasting for two or three days, and only falling towards the end, or when recovery occurs. Thus, instead of the above proportion 18 : 100, the proportion to the total nitrogen rose in individual cases as high as 27, 31, 57, and even as high as 83 per cent. In one case it rose from 18 per cent on the day of poisoning to 97. These changes in phosphoric acid excretion are probably to be referred, not to any oxidation of the phosphorus taken, but to a great destruction of phosphorus-containing tissues—chiefly of the liver. Phosphorus exercises no special destructive action on the red corpuscles, one source of lecithin. On the other hand, it has been found by Heffter that the lecithin of the liver after phosphorus poisoning is reduced by one-half.

Sulphuric acid.—The excretion of this acid in phosphorus poisoning corresponds in the main to that of phosphoric acid. It is increased. A large increase of the unoxidised compounds of sulphur was found in a case recorded by Starling and Hopkins. A similar change was noted by Goldmann in some cases of phosphorus poisoning.

As regards the *ether sulphates* they seem to vary ; sometimes they are increased. In one case the proportion of ether sulphates to the inorganic sulphates was 1 to 5·9, instead of 1 to 10 as in health. On the other hand, they have been found diminished, for example, 1 to 20 (Starling and Hopkins), 1 to 54·6 (Munzer).

Morbid anatomy.—The chief changes found post-mortem are (i.) *jaundice;* (ii.) *hæmorrhages*, usually small and punctiform, scattered over the various serous membranes—pleura, pericardium, mesentery, and in the mucous membrane of stomach and intestine, under the skin and between the muscles; sometimes of larger size, and met with in the liver, and in the tissues of the neck and elsewhere.

(iii.) *Fatty degeneration of liver and kidneys.*—The *liver* is usually considerably enlarged and remarkably fatty, presenting all the characters of a fatty liver—doughy to the feel, greasy on section, its lobules indistinct and deeply bile-stained. Its colour is usually a uniform pale yellow ; but in some cases there are portions here and there of a more reddish yellow colour, due to congestion of the centres of the lobules. On microscopic examination the liver-cells are found fattily degenerated, their outlines indistinct, the nuclei refusing to stain, and the substance of the cell converted into fine granular detritus, or filled with large fat drops, especially in the outer zone of the lobule. The cells of the central zone often contain biliary pigment. The connective tissue throughout the liver is usually unaffected ; in a few cases it has been found in a state of proliferation. In rare cases the liver may be found diminished in size and shrunken, instead of increased. The increase of fat is very notable. The normal liver contains about 3 per cent of fat, 76 per cent of water, and 21 per cent of non-fatty substance. In phosphorus poisoning the percentage of fat is as high as 30, water 60, and non-fatty tissue 10 per cent. This increase of fat contrasts remarkably with what is found in *acute yellow atrophy; namely,* 4·2 *per cent of fat,* 80·5 *per cent of water,* and 15·3 per cent of non-fatty substance.

The *kidneys* are usually swollen, soft, and enlarged; the capsule strips off easily; the cortex is increased in thickness, and pale, contrasting with more purple colour of the medulla. On microscopic examination the epithelium of the convoluted tubules is swollen and fatty, or thrown off as casts.

The *heart* is flabby, and its muscle presents a more or less mottled appearance from fatty degeneration.

The *spleen* is usually enlarged, often to double its natural size, and full of blood; in other cases it is small and firm.

Nature of the jaundice.—This problem is one of peculiar interest Far more than any other form of jaundice, that of phosphorus poisoning has long been held to establish the existence of a jaundice from suppression independent of obstruction. The facts in favour of such a view are that the bile-ducts, or at least the larger bile-ducts, are free from obstruction, often indeed free from bile; the blood shows no evidence of any special destructive action of the poison, such as we meet with in the case of other icterogenetic poisons; and, lastly, the intense fatty change in the liver indicates that the poison acts specially on the liver-cell.

What more reasonable, then, than to conclude that the function of the liver has been "suppressed," and that jaundice is one of the results.

Nevertheless the evidence adducible appears to me conclusively to show (*a*) that at the time at which the jaundice occurs the functions of the liver are by no means suppressed, however much they may be, and doubtless are, injuriously affected; and (*b*) that the changes in the bile (increased viscidity and retarded flow) are such as sufficiently to account for the jaundice (Stadelmann)—changes similar in character, though less in degree than those produced by toluylendiamin.

So far as total suppression of function is concerned, the excretion of urea, and more especially the relative proportions of urea and ammonia in the urine, afford an important index to the activity of the liver. If the liver be cut off from the circulation, and its functions thus suppressed, there is a great fall in the amount of urea, and a no less marked increase in the ammonia of the urine.

In disease a suppression of its function, such as is assumed to occur, ought to manifest itself in the same way, namely, (*a*) by a great fall in the total excretion of urea, (*b*) by a large proportionate increase in excretion of ammonia. Yet as a matter of fact the elaborate analyses of Münzer show that so far from urea being reduced to vanishing-point, urea continues to be excreted in quantities approximating to those of health—in quantities, therefore, which, when we consider the absence of food, greatly exceed those of health.

Moreover, and still more significant of continued activity of the liver, urea still constitutes about 80 per cent of the total nitrogenous excretion (instead of the normal 90 per cent)—the increase in ammonia being only moderate (10 to 18 per cent instead of the normal 4 to 6 per cent).

This increase in the percentage of ammonia might be taken as an indication of some impaired activity of the liver in transforming ammonia into urea. But even this significance cannot be attached to it. Both Starling and Hopkins, who had previously described it, and Munzer are in accord in referring it rather to the increased acidity which is a feature of the blood (as also of the urine) in phosphorus poisoning (von Jaksch); and the experiments of Munzer have confirmed the accuracy of this view.

Whether, then, we have regard to the increased formation and excretion of bile pigments shown by Stadelmann's experiments to occur in the first stage of the poisoning, or the continued formation of urea which occurs throughout almost up to the last moment, there is at the time at which the jaundice occurs absolutely no evidence of the total arrest or suppression of function which the suppression theory contemplates

On the other hand, there is at the time at which the jaundice appears evidence of marked fall in the quantity of bile—one-fifth its former amount, with an increase of its viscidity sufficient of itself to retard and temporarily to arrest the flow of bile in the small bile-ducts. And indeed changes in those ducts have long been noted and described. Thus Oscar Wyss (1867), in experiments on dogs, found the larger ducts free from bile and unstained, while the smaller ones were filled with thick mucus which prevented the flow of the bile downwards. And similar appearances have been noted in man (Ebstein), although others have failed to find them (Schultzen and Riess).

Considering the obvious effects of the poison on the liver-cell (swelling and fatty degeneration), it is not difficult to understand how an analogous injurious effect on the lining of the smaller bile-ducts may lead to swelling and increased secretion sufficient to retard or arrest the flow of bile along them.

To sum up, then: the jaundice of phosphorus poisoning is essentially obstructive; it is *hæmo-hepatogenous* in nature, and is due to obstruction in the smaller bile passages set up by changes in its epithelium and in its secretion.

THE JAUNDICE OF YELLOW FEVER.—For a full description of yellow fever the reader is referred to the article on the disease in the second volume (p. 385). So far as the jaundice is concerned, the disease bears a striking resemblance to cases of so-called *icterus gravis* observed from time to time in this country. The symptoms of these maladies are closely alike. Indeed, isolated cases of yellow fever are not to be distinguished from cases of icterus gravis.

Yellow fever presents characters of acute yellow atrophy—the same mode of onset, with fever and slight jaundice followed suddenly by the severer symptoms of black vomit, hæmorrhage, delirium, convulsions, coma, and death. The close resemblance has been noted by all observers, and a few have even gone so far as to regard the two diseases as identical (Liebermeister). However, the facts hardly bear out such a conclusion. Although of the same generic character, the changes in the liver in the two diseases are not quite identical. In both cases they indicate the action of a severe poison; but the characteristic atrophy found in acute yellow atrophy points to the action of a more virulent poison than that present in yellow fever. In the latter disease there is not the shrinking of the liver which is so marked a feature of the former.

In both diseases we have to deal with the action of poisons closely similar in nature and action, although not identical. And the same conclusion probably applies to yellow fever and icterus gravis. The resemblance is here absolute in all points—both in the clinical features during life, and in the post-mortem changes after death.

An isolated case of yellow fever occurring in this country would, apart from any history of its importation, be almost certainly regarded as a case of icterus gravis.

REFERENCES

1. AFANASSIEW. *Zeitschrift f. klin. Med.* vi.—2. *Idem.* *Virch. Archiv*, xcviii. p 465, 1884.—3. AULD, A. G. "On Hæmatogenous Jaundice," *Brit. Med. Jour.* i. 1896, p. 137.—4. BRUNTON, LAUDER. *Handbook for Physiolog. Labor.* 1873, p. 499.—5 CHAUFFARD. "Maladies du Foie," *Traité de médecine*, 1892, p. 704.—6. COPEMAN. "The Crystallisation of Hæmoglobin in Man and the Lower Animals," *Jour. of Physiol.* xi. 1890; *Lancet*, i. 1887; *Brit. Med. Jour.* ii. 1889, p. 190.—7. CULLEN. *Works*, vol. ii. p. 656, 1827.—8. FRERICHS. *Diseases of the Liver*, 1858.—9. GAMGEE. *The Physiological Chemistry of the Animal Body*, vol. ii. 1893.—10. GARROD, A. E. "On the Occurrence and Detection of Hæmatoporphyrin in the Urine," *Jour. of Physiol.* xiii 1892.—11. GARROD, A. E., and HOPKINS, F. GOWLAND. "On Urobilin," *Jour. of Physiol.* xx. 1896.—12. HARLEY. *Diseases of the Liver.* London, 1880.—13. HAYEM. *Du Sang.* Paris, 1889.—14. HUNTER, WILLIAM. *Thesis*, University of Edinburgh, 1886. -15. *Idem.* "The Physiology and Pathology of Blood Destruction," *Lancet*, ii. 1892.—16. *Idem.* "The Action of Toluylendiamin," *Jour. of Pathology and Bacteriology*, vol. iii. 1895 —17. *Idem.* "Excretion of Pathological Urobilin in Pernicious Anæmia," *Practitioner*, 1889.—18. KÜHNE. *Virchow's Archiv*, xiv. p. 337, 1858; *Lehrbuch d. phys. Chemie*, Leipzig, 1868.—19. LEGG, WICKHAM. *The Bile, Jaundice, and Bilious Diseases.* London, 1880.—20. LEYDEN. *Beitrage zur Pathologie des Icterus*, 1866.—21. LOWIT. "Beitrage zur Lehre vom Icterus," Ziegler and Nauwerk's *Beitrage zur pathol. Anat.* iv.—22. MACMUNN. "On the Origin of Urohæmatoporphyrin and of Normal and Pathological Urobilin in the Organism," *Jour. of Physiol.* x. 1889.—23. MINKOWSKI and NAUNYN. "Ueber den Icterus durch Polycholie und die Vorgange in der Leber bei demselben," *Archiv f. exp. Pathol. u. Pharmak.* xxi. 1886.—24. MOXON. *Trans. Path. Soc. Lond.* 1873, xxiv. p. 133.—25. MÜNZER. "Der Stoffwechsel des Menschen bei acuter Phosphorvergiftung," *D. Archiv f. klin. Med.* xxii. 1894.—26. MURCHISON. *Diseases of the Liver*, London, 1868, 3rd edition, edited by T. Lauder Brunton. London, 1885.—27. NAUNYN. "Beitrage zur Lehre vom Icterus," *Archiv f. Anat. u. Physiol.* 1868, p. 401.—28. NEUMANN. "Beitrage zur Kenntniss der pathologische Pigmente." *Virch. Archiv*, Bd. ii. C. xi.—29. QUINCKE. *Virch. Archiv*, Bd xcv.—30. SAUNDERS. *The Structure, Economy, and Disorders of the Liver.* London, 1809.—31. SILBERMANN. "Ueber Haemoglobinaemie," *Zeitschrift f. klin. Med.* 1886, xi. p. 471.—32. STADELMANN. *Der Icterus und seine verschiedenen Formen.* Stuttgart, 1891.—33. *Idem.* "Zur Kenntniss der Gallenfarbstoff Bildung," *Archiv f. exp. Path. u. Pharmak.* 1882, xv. p. 337.—33*a*. v. STORCK. "Beitrage zur Path. der Phosphor Vergiftung," *D. Archiv f. klin. Med.* xxxv. 1884.—34. STARLING and HOPKINS. "Note on the Urine in a Case of Phosphorus Poisoning," *Guy's Hosp. Rep.* xlvii. 1890.—35. STEINER. "Ueber de haematog. Bildung des Gallenfarbstoffes," *Arch. f. Anat. u. Physiol.* 1873.—36. STERN. *Arch. f. exp. Path. u. Pharmak.* xix. p. 39.—37. TARCHANOFF. "Ueber die Bildung von Gallenpigment aus Blutfarbstoff im Thierkorper," *Pfluger's Archiv*, Bd. ix.—38. VIRCHOW. *Virch. Archiv*, i. p. 1; *Ibid.* xxxii.

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WEIL'S DISEASE

SYNONYMS.—*Infectious jaundice*, *Febrile jaundice*.

IN 1886, under the title of "A peculiar form of acute infectious disease characterised by Jaundice, swelling of Spleen, and Nephritis," there appeared a paper by Professor Weil of Heidelberg, describing four cases of febrile jaundice presenting certain general features of resemblance. He was in doubt whether to regard them as extremely rare modifications of other well-known forms of infectious disease, or, on the other hand, as a disease hitherto unrecognised. The paper excited much interest, chiefly amongst German observers, who decided at once in favour of the latter alternative, and gave it the title of "Weil's disease."

Since then a considerable discussion has sprung up in connection with the subject—almost exclusively amongst German writers. French observers have, for the most part, declined to see in the condition anything more than what they had long been accustomed to describe under the title of icterus gravis, or infectious jaundice; and, judging from the attention bestowed on it, the same view appears to have been taken by most English and American observers.

Symptoms.—The character of the disease in Weil's original cases was that of a sharp febrile attack coming on suddenly, with or without rigors, followed on the second or third day by jaundice, swelling of liver and spleen, and nephritis; marked by severe nervous symptoms, and ending gradually in recovery about the tenth or fifteenth day.

The disease begins with fever with or without rigors, extreme debility and general malaise, painful sensations or violent muscular pains in back and limbs, loss of appetite, thirst, usually diarrhœa, headache, giddiness, and disturbed sleep. These symptoms increase in intensity for a day or two, the weakness becomes more marked, and to the other nervous disturbances there are added slight delirium and somnolence. On the second or the third day jaundice appears, with marked swelling and tenderness of the liver and enlargement of spleen; and the urine becomes albuminous, and shows the other changes characteristic of nephritis. In the digestive system the disturbances are very marked—furred tongue, sometimes vomiting, diarrhœa, or constipation, sometimes abdominal pains and uneasiness.

All these symptoms continue for two or three days more, and then gradually subside, improvement setting in on the fifth to the eighth day. The temperature, which has remained high, falls gradually to the normal about the tenth day, the jaundice gradually disappears along with the other symptoms, and convalescence begins.

The convalescence may be uninterrupted; but in a certain number of cases, after an apyrexial period of one to seven days, fever recurs, lasting five or six days, sometimes, though exceptionally, attended with recurrence of jaundice, swelling of liver and spleen, and albuminuria.

Convalescence is in all cases slow, the patients being left much reduced in strength for many weeks after.

The jaundice is the most striking symptom of the disease. It usually shows itself about the second or third day, and rapidly increases till, in the course of twenty-four hours, the patient is quite yellow. It lasts about fourteen days, and disappears slowly. Bile pigments are abundantly present in the urine; bile acids are also sometimes present. It is attended by *swelling and tenderness of liver*, corresponding in degree to the degree of jaundice, and gradually disappearing with the latter.

In all cases there is also notable *enlargement of spleen*, recognisable at the very outset of the fever even before the jaundice appears, and lasting as long as the fever lasts.

The fever is a constant symptom and is usually high, reaching 103° or 104° F. in the course of the second or third day, and, with slight morning remissions of about a degree, it remains high for several days. Then between the fifth and ninth days it begins slowly to fall, and reaches the normal about the ninth or twelfth day. In about three-fourths of the cases the temperature then remains normal. In the remaining fourth, after a few days' intermission, it rises again for several days, sometimes even reaching its former height. It is only in exceptional cases that this recurrence of fever is attended by jaundice, swelling of the liver and spleen, and albuminuria.

The pulse corresponds to the fever, is usually rapid—110 to 120, sometimes even 136. When jaundice appears it becomes slower.

Nervous symptoms are very prominent and constant. They include headache, giddiness, great prostration, and more or less delirium. But perhaps the most striking symptom of all are the muscular pains, especially in the calves of the legs; these are sometimes so severe that they put the other subjective symptoms into the background. The pains occur spontaneously, and are greatly increased by movements and by palpation of the muscles.

Nephritis is almost constant, and is evidenced by albuminuria, presence of epithelial casts, and sometimes blood. Its occurrence coincides with the enlargement of the spleen, and it usually subsides with the latter. Some albuminuria often persists for a long time during convalescence.

Occasional symptoms observed have been *rashes*, roseola, erythema, purpura, herpes, and in a few cases *epistaxis*.

Etiology.—The disease has been most commonly met with in men between the ages of fifteen and thirty; a few cases have occurred in children between eight and fourteen. The greatest number have occurred in the summer months between June and September, but isolated cases have been met with in winter and spring.

It is not confined to any one class of society, but it is certainly most common in working-men (thirty-eight out of fifty-three) whose occupations or habits have exposed them to insanitary surroundings.

Infection undoubtedly plays the most important part in producing it. Thus out of thirteen cases recorded by one observer (Fiedler), nine were in men engaged in the slaughter-house of Dresden, and two of the others had eaten tainted sausage. Two cases described by another observer (Stirl) were in workmen engaged in cleaning out a sewer, who were taken ill with all the symptoms of the disease. Ducamp reports on a slight epidemic outbreak of infectious jaundice in six workmen who fell ill after cleaning out a blocked sewer, three of them of gastric catarrh, three of Weil's disease.

Lastly, a series of epidemic outbreaks of the disease have been recorded, chiefly by garrison officers in Germany.

Thus under the title of "infectious jaundice" an outbreak of jaundice was recorded in 1866 by Weiss,—twenty-five cases observed by himself, and fifteen others known to him,—presenting in all respects the characters of Weil's disease. In one instance the father and two sons of a single family were attacked successively. Similar outbreaks have been recorded by Haas (1887) and Weiss (1889), both in Prague; and by Pfuhl (1888), Hueber (1890), and Jaeger (1892). The last observer has reported nine cases—three of them fatal—occurring in garrison at Ulm; the source of infection was traced by him to bathing in a certain part of the river near the garrison. A similar outbreak in a garrison was traced to bathing, and reported by Globig (1890).

Pathogeny.—As to the nature of the infection observations are still wanting. In the outbreak recorded by him Jaeger succeeded, in two out of three fatal cases, in discovering within the organs of the body a certain organism, with definite morphological and cultural characters, which he believes to be the cause of the disease. To this he gives the name "Bacillus proteus fluorescens." He found the same organism in the urine in four out of six of the patients who recovered, whereas he failed to find it in a case of simple catarrhal jaundice. On further investigation he ascertained that on the banks of the infected river running past the garrison where the disease was acquired by bathing, the water-birds—ducks and geese—frequenting the river were subject to a fatal disease marked by jaundice, and on examination he found the same post-mortem changes and the same organism present in them.

In two fatal cases recorded by him Nauwerck had already (1888) found organisms in the intestinal wall—partly within the glands, partly amidst the connective tissue—apparently within widened lymphatics, and forming zoogloea-like masses made up of small bacilli, with rounded ends deeply stained; the middle portion being hardly stained at all. Jaeger recognises in the description the same organism he also had found.

Morbid anatomy.—The disease is not usually fatal; and hence only a few records of post-mortem examination are available, ten in all—three recorded by Sumbera, two by Nauwerck, one by Brodowski and Dunin, three by Jaeger.

The following was the condition observed by Sumbera in three fatal cases. In all there was jaundice with fatty degeneration of the heart-muscle, and numerous punctiform hæmorrhages either under the skin, the pericardium, the pleuræ, or the mucous membrane of intestine.

CASE 1.—*Liver* deeply bile-stained; lobules indistinct; liver-cells showing cloudy swelling; fatty infiltration of periphery of lobule; connective tissue not increased.

Spleen: not enlarged.

Kidneys: large and soft; numerous punctiform hæmorrhages in cortex, epithelium degenerated.

Duodenum: mucous membrane swollen and studded with hæmorrhages.

Dura mater: inner surface covered with a hæmorrhagic membrane.

CASE 2.—*Liver* large, firm, deeply jaundiced; liver-cells cloudy nuclei considerably increased.

Gall-bladder and bile-ducts: mucous membrane swollen and hyperæmic.

Spleen: large, soft.

Kidneys: parenchymatous nephritis.

Bladder contained urine and blood.

Stomach and intestine: mucous membrane throughout hyperæmic and catarrhal, and studded with hæmorrhages.

CASE 3.—Intense jaundice. Changes in heart, liver, spleen, kidneys, stomach, and intestine same as in Case 2.

Blood and organs were examined for organisms but with negative result.

Three fatal cases have been recorded by Jaeger. The chief changes were jaundice; fatty degeneration of liver with indistinctness of lobules, and small cell infiltration of connective tissue; fatty degeneration and cloudy swelling of epithelium of kidney and acute parenchymatous nephritis, minute hæmorrhages in different organs; swelling of spleen; intestinal changes, observed in one case only but in this one very notable, namely, marked vascularity, numerous hæmorrhages, and superficial erosions of mucous membrane throughout whole intestinal tract. No trace of typhoid lesion ever observed. In two out of the three cases Jaeger found a definite organism in the tissues as already noted. Similar changes were described in the two cases by Nauwerck (1881). The changes in the liver are described by him as resembling those of acute yellow atrophy in many respects; liver-cells reduced to a granular fatty detritus; the epithelium of bile-ducts fattily degenerated to a high degree. In the intestine nothing special was noted. In both cases he found an organism in wall of intestine.

Nature and relation to other forms of jaundice.—The infective nature of the disease can hardly be doubted. The sudden onset and the character and course of the symptoms suggest this; and its occasional occurrence in epidemic or endemic outbreaks seems to establish it conclusively. In one instance the father and the two sons of one family were attacked successively. Beyond this its etiology is quite obscure; how much so may best be judged from the different names given to the condition by different observers.

Weil gave it no name at all. He was not sure whether to regard it as a special disease, a form of "bilious typhoid," or as a form of abortive enteric fever. And on these points the opinions of German observers, among whom, as I have said, the condition has received most attention, appear greatly divided — "Infectious or septic jaundice" (Fraenkel); "Febrile jaundice" (Wagner); "Infectious jaundice" (Wassilieff, Weiss); "Icterus typhosus" (Heitler); "Abortive enteric fever" (Haas); "Typhus biliosus nostras" (Weiss).

The term "bilious typhoid" has been given to it on the ground that its characters agree generally with those formerly described by Griesinger under the name "typhus biliosus." Moreover, it has been thought to be identical with the disease described as "typhus biliosus or icterodes" met with in Alexandria and Smyrna. The name appears to me, however, to be particularly inapplicable. For later observers have shown that the disease described by Griesinger was really relapsing fever; in which disease jaundice occurs in a large proportion of cases (over 37 per cent) [vol. i. p. 943]. And there are important differences between it and the Smyrna disease; in the latter the spleen is usually normal, parotitis is common, and over 27 per cent of cases prove fatal.

The disease cannot be regarded as an abortive form of enteric fever. Jaundice is one of the rarest complications of enteric fever. Murchison met with only 4 cases; Jenner never with one; Liebermeister with 26 out of 1420 cases; Griesinger with 10 out of 600 cases. Moreover, when jaundice does occur it is not, as in the condition now under consideration, at the outset of the disease.

Lastly, in the necropsies recorded typhoid lesions have not been noted.

These possibilities being excluded, there remains only the question whether the condition is to be regarded as a special disease, or as one form of "infective jaundice." The evidence appears to me to be against the former and in favour of the latter view.

The closest relations of the disease appear to be with other forms of "infective" jaundice such as are met with sporadically or endemically both in this country and abroad, and more especially with sporadic forms of yellow fever in America. And it is of interest to note that I find no mention of Weil's disease by physicians in America, where febrile forms of jaundice are so common; or by physicians in Australia, in certain parts of which (Broken Hill) febrile jaundice appears to be almost endemic.

Neither in the symptoms nor in the morbid changes described as Weil's disease is there anything essentially characteristic. They are those of a severe icterogenetic poison, more severe than that found in epidemics of ordinary catarrhal jaundice, and in most cases not so severe as that observed in cases of "malignant" jaundice (icterus gravis). Its relations to both these varieties of jaundice are, however, manifest. Thus I find four cases recorded (von Fetzer, 1882) amongst soldiers, three in

August and one in September, in certain rooms of a barrack in which there had been an outbreak of epidemic (catarrhal) jaundice from February to June of the same year; one of those attacked in August having suffered from "catarrhal" jaundice in June. On the other hand, *the symptoms and post-mortem appearances in severe fatal cases are absolutely indistinguishable from those of severe cases of icterus gravis.* In two of Jaeger's cases even tyrosin crystals were found in the urine.

It appears to me, then, that until the nature of the infecting agent can be determined, no advantage is to be gained from regarding a condition which probably owes its origin to different infective agents in different localities as a special disease, or in giving to it the name of any one observer.

The older name of "infectious jaundice" serves sufficiently to describe it.

As regards the character of the jaundice itself, it remains to point out that there is a striking similarity between it and that producible experimentally in dogs by toluylendiamin. Great swelling of spleen and liver and nephritic changes are constant features of the action of this drug When large doses are given I have found that considerable fever is also present.

Post-mortem the changes are identical, the bile-ducts being distended with bile; and, most striking of all, the duodenum shows in certain cases the marked congestion which I have described as characteristic of the action of toluylendiamin.

REFERENCES

1. Brodowski and Dunin. "Ein Fall der sogen. Weils'chen Krankheit mit lethalem Ende," *D. Archiv f. klin. Med.* xliii.—2. Fiedler. "Zur Weils'chen Krankheit," *D. Archiv f. klin. Med.* Bd. xlii. 261.—3. Fraenkel. "Zur Lehre von der sogenannten Weil'schen Krankheit," *Berl. klin. Woch.* 1889, No. 33.—4. Goldenhorn. "Zur Frage ueber die Weils'chen Krankheit," *Berl. klin. Woch.* 1889, No. 33.—5. Goldschmidt. *D. Archiv f. klin. Med.* Bd. xl. S. 238.—6. *Idem.* "Ein Beitrag zur neuen Infectionskrankheit Weils."—7. Heitler. "Zur Klinik des Icterus Catarrh," *Wien. med. Woch.* 1887, No. 30.—8. Mathieu. "Typhus hépatique bénin," *Revue de méd.* 1886, ii. 633.—9. Nauwerck. "Zur Kenntniss der fieberhaften Gelbsucht," *Munch. med. Woch.* 1888, No. 35.—10. Wagner. "Zwei Falle von fieberhaften Ikterus," *D. Archiv f. klin. Med.* Bd. xl. p. 421, 1887.—11. Wassilieff. "Ueber infektiosen Ikterus," *Weiner Klinik*, 1889.—12 Weil. "Ueber eine eigenthumliche, mit Milztumor, Ikterus und Nephritis einhergehende akute Infectionskrankheit," *D. Archiv f. klin. Med.* xxxix. 1886.—13 Weiss. "Zur Kenntniss und zur Geschichte der sogenannten Weils'chen Krankheit," *Wien. med. Woch.* 1890, Bd. xl. 425, 470, 516, 557, 611.—14. Windtscheidt. "Zwei Falle von Weils'chen Krankheit," *D. Archiv f. klin. Med.* Bd. xlv. S. 132.—15. Young, E. H. "Notes on a Case of Weil's Disease," *Lancet*, 1889, ii. 1109.

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ACUTE YELLOW ATROPHY OF LIVER

SYNONYMS.—*Ictère grave*, *Icterus typhoides* (Lebert), *Acute parenchymatose Hepatitis* (Foerster), *Ictère hémorrhagique essentiel* (French authors), *Parenchymatose Degeneration der Leber* (Liebermeister).

Definition. — An acute disease, probably of toxic origin, characterised by jaundice in association with severe cerebral symptoms, black vomit, and hæmorrhages; and by marked diminution in the size of the liver due to parenchymatous degeneration.

History.—The disease was probably not unknown to earlier writers, but only a few cases, and these of doubtful nature, are recorded until early in the present century. According to Dr. Wickham Legg, no record of any case is to be found earlier than 1616. One of the first to record cases presenting the features of this disease was Morgagni. Early in this century observations were made by the Dublin physicians, Cheyne (1818), O'Brien (1818), and Marsh (1822); and in Edinburgh by Abercrombie (1828). One of the earliest and fullest accounts of the disease, however, was that given by Bright (1836); he described it as a diffuse "inflammation" of the substance of the liver affecting the glandular substance more than the connective tissue, leading frequently to marked diminution in the size of the organ, causing jaundice associated with severe nervous symptoms, and a special tendency to hæmorrhage. Bright's account must be regarded as the earliest recognition of the disease as a definite symptom group. He regarded it as a "diffuse inflammation."

The history of the disease, under the title it now bears, dates from 1843, in which year Rokitansky, basing his description mainly on the naked-eye appearances presented by the organ, described it under the name "acute yellow atrophy."

It was not till a few years later that the characteristic microscopic appearances, significant of degeneration of the liver-cells, were described; first of all by two English observers—Busk (1845) and Handfield Jones (1847).

In France the first full account of the disease was given by Ozanam (1849), under the title of a "forme grave de l'ictère essentiel."

From this time onward observations accumulated. Lebert's account of the disease (1854) was based on a study of seventy-two recorded cases of *icterus gravis*, many of them of doubtful nature. He regarded the condition as a general disorder rather than as a special disease of the liver, and preferred to name it *icterus typhoides*; this view was propounded about the same time by Buhl also.

In the first edition of his well-known work on *Diseases of the Liver* (1858), Frerichs gave an account of the disease based on a study of *thirteen cases which had come under his own observation, and thirty-one recorded cases.*

Later important contributions to the study of the disease were made by Wunderlich (1860), Wagner (1862), Liebermeister (1864).

The remarkable similarity between the morbid changes found in the liver and kidney in this disease and those produced by phosphorus poisoning was first pointed out by Rokitansky (1860). Wagner was the first to suggest that many cases of the disease might really be unrecognised cases of phosphorus poisoning.

Liebermeister's contribution was an important one. He described ten cases observed by himself, and made a study of all the cases of *icterus gravis* on record (177 in number recorded by eighty-two authors), fitted to throw any light on the relation between that condition and acute yellow atrophy.

Amongst more recent accounts the two fullest and best are those given by Wickham Legg (1880) and Thierfelder (1880); the latter based on a study of 143 cases recorded up to the year 1876, the former on 100 cases recorded up to the same date (1876-77).

The present account is based mainly on fifty cases which I have collected in the records from 1880 to 1894 inclusive.

Etiology.—Acute yellow atrophy must be ranked amongst the rarest of diseases. It is seldom met with even in the largest hospital practice. Out of 25,700 cases admitted during nine years into the London Fever Hospital at a time when a brown tongue and delirium constituted a sure passport to admission, Murchison states he only met with one case. Wickham Legg found only one case in the course of nine years at St. Bartholomew's Hospital. Thierfelder estimates with some probability that the total number of recorded cases up to the year 1880 does not exceed 200.

Since then, between the years 1880 and 1894 inclusive, I have been able to collect some fifty additional cases, thus bringing the total up to 250. As regards the rarity of the disease Liebermeister's experience must be regarded as exceptional. No fewer than ten cases, confirmed by autopsy, came under his observation in a comparatively short period, and he stands alone in regarding the disease as one comparatively common. It is probable that amongst this number were some which ought to be grouped as cases of *icterus gravis* rather than as acute yellow atrophy. This appears the more likely, as Liebermeister considered the chief criterion of the existence of the disease to be the occurrence of "parenchymatous degeneration" of the cells of the liver, a pathological condition by no means confined to acute yellow atrophy.

Age.—Acute atrophy is most commonly met with betwixt the ages of 20 and 30 (50 per cent), but no age is exempt. It is very rare in childhood below the age of 10; 8 cases out of 143 collected by Thierfelder, 7 out of 100 collected by Wickham Legg, 2 out of 63 collected by Lebert, 4 out of 37 collected by myself occurred in patients under 10 years of age.

The earliest age recorded is that of an infant taken ill four days after birth (Politzer). Of the four recent cases I have collected, one was aged 2¼ (Goodhart, 1881), one aged 7 (Venn, 1884), one aged 6 (Ross, 1888), and one aged 10 months (Yeoman, 1892).

One-half of the cases have occurred between the ages of 20 and 30, more than four-fifths between the ages of 10 and 40. Below 10 and above 40 the number rapidly diminishes.

Sex.—The influence of sex is undoubted; one of the few facts definitely established as regards the etiology of the disease is that females greatly preponderate among those attacked. Between the ages of 20 and 40, when the liability to the disease is greatest, the proportion of females to males attacked is exactly double. This greater liability is connected with the occurrence of pregnancy. Out of 49 cases recorded by Thierfelder in women, 18 occurred in pregnant or lying-in women. Out of Frerichs' 31 cases, 22 were women and 11 of these were pregnant. Out of 69 cases in women collected by Wickham Legg, 25 were in pregnant women. Out of 42 recent cases collected by myself, 24 were in women; and of these 12 were pregnant, or suckling. It occurs in every stage of pregnancy except the first three months, but is most common about the middle period. The greater disposition to the disease thus shown by pregnant women is probably related to the fact first observed by Virchow (1848), namely, that a certain degree of parenchymatous degeneration of the liver and renal cells is a common condition in pregnancy. Even in pregnant women, however, the disease is of very rare occurrence—only 1 in 28,000, according to one observer (Braun), or 2 in 33,000 (Spaeth). Pregnant and suckling women show a similar liability to be attacked by other severe forms of jaundice—notably that occurring in epidemics.

Seasons.—Season of the year is without any influence. It is met with alike in extremes of heat and of cold.

Constitution.—The majority of cases occur in those of robust constitution, a certain number in persons weakened by excess; this latter number is not so great as to suggest any special relation between weakened constitution and liability to the disease.

Syphilis.—No definite relation can be traced between syphilis and the disease.

Alcohol.—Nor can any definite part in the causation of the disease be assigned to alcohol. A certain number—in Thierfelder's cases 13 out of 143—occurred in patients who were or had been heavy drinkers; and in some cases—6 out of the foregoing 13—the attack had followed a period of unusually heavy drinking. As pointed out by Liebermeister, the habitual use of alcoholic drinks favours a certain degree of parenchymatous degeneration of the liver.

Other hepatic diseases.—The disease occurs not only primarily, as an acute process in persons previously in good health, but also secondarily, in persons already the subject of liver disease. A certain number of cases are recorded in which it occurred secondarily to, or was superadded to cirrhosis of the liver, long persistent biliary obstruction, or chronic fatty degeneration. Amongst more recent cases, as in one recorded by Dr. Cayley, it supervened on a chronic cirrhotic process, the result of free drinking, in a case of somewhat doubtful nature, a child aged 7, it followed hypertrophic cirrhosis.

There is no evidence, however, that these morbid conditions—which after all are relatively very common—have any special causative relation to the disease, except in so far as they induce an unhealthy state of the liver-cell.

Mental emotion.—That an antecedent morbid condition of the liver-cell is not necessary for the occurrence of the disease is in no wise more clearly evidenced than by the fact that in the great majority of cases, as I have said, it attacks people previously in robust health; and in a considerable proportion of these cases the only cause assignable has been the influence of fright or some depressing mental emotion. Out of Lebert's 72 cases, 13 were assigned to the latter cause; 16 out of 100 cases collected by Wickham Legg; and one-tenth of the cases according to Thierfelder. Most of these cases were in women. It is on the basis of such cases some authors have surmised that acute yellow atrophy is a nervous disease (von Dusch), or at any rate that depressing emotion plays a pre-eminent part in its causation (Liebermeister). Among recent cases I find only two ascribed to mental shock,—one in a pregnant woman aged 24 (Hayward, 1890); one in a man aged 41 recorded by Duckworth. This man saw his own child run over in the street; on the following day he became jaundiced, and four weeks later the acute symptoms set in. Such an ascription has, however, but little in its support.

Toxic influences.—It is when we come to discuss the relations of acute yellow atrophy to other forms of severe jaundice that we find some light thrown on the probable etiology of the disease. The condition of liver and kidney in acute yellow atrophy, as first pointed out by Rokitansky, closely resembles that induced by phosphorus poisoning. Moreover, certain symptoms are common to the two affections, those which are constant in the one being constant in the other; while the inconstant symptoms occur in both with about the same relative frequency. It has been suggested, accordingly, that some cases of the disease under discussion may really be obscure cases of phosphorus poisoning; by some writers, indeed, it has been urged that all cases have this origin.

The resemblances—namely, the parenchymatous changes in liver and kidney attended by jaundice and severe nervous symptoms—are undoubtedly so striking as to suggest that the one disease like the other has a toxic origin; yet there are certain differences which appear no less clearly to denote that the two diseases are not identical. Thus, as regards the size of the liver, out of 15 cases of phosphorus poisoning, collected by Lewin, in which the condition of liver was noted, in no case was it diminished; in 4 it was normal, and in no fewer than 11 it was actually enlarged. Moreover, even as regards the prominent feature—jaundice—recorded experiences are rare. Out of 20 cases collected by Liebermeister, in only one was it missed. On the other hand, Lewin found it present in a minority of cases only—15 out of 44; and Ehrle, likewise, in 8 cases out of 23. And there are minor differences between the two conditions; especially as regards the characters of the urine and the general character of the nervous symptoms.

On the whole, then, taking the most liberal interpretation of the relationship between acute yellow atrophy and poisoning by phosphorus, we should have to conclude that the former must be an anomalous form of poisoning by the drug—a conclusion, I need hardly say, somewhat different from the allegation that the two affections are identical. The resemblances between the two conditions, such as they are, nevertheless lend strong support to the view that acute yellow atrophy, if not due to phosphorus, is due to some toxic agent.

Further support is lent to this opinion when we consider the close affinities between the disease and other forms of severe jaundice, where the action of specific poisons is less doubtful; such, for example, as yellow fever and severe cases of *icterus gravis*. The resemblance between yellow fever in particular and acute yellow atrophy are many and striking, so many as even to suggest to some observers that the latter may be nothing more or less than sporadic cases of the former.

And so it is with regard to other forms of severe jaundice—*icterus gravis*—whether occurring sporadically or in epidemic form. Many such outbreaks of *icterus gravis* have now been recorded, sometimes widespread, sometimes limited to one single household; and the more severe of these cases present many of the features of acute yellow atrophy, including the nervous disturbances, the hæmorrhages, and so on. Thus Budd observed several cases of severe jaundice on board a ship: one fatal case showed parenchymatous degeneration of the liver-cells; in another, where recovery eventually took place, severe nervous symptoms and bloody stools were present. Three very striking cases of the same kind, and occurring in one family, I find recorded by Graves in his *Clinical Lectures*. The first case was a girl aged 17, who was suddenly seized with vomiting and jaundice; on the fifth day she became comatose, had convulsions, and died on the day following. Nine months later her sister aged 11 suddenly fell ill, became jaundiced on the third day, vomited black matter, became insensible and convulsed, and died on the fourth day. The liver was found of normal size, but soft in consistence, the cut surface presenting a peculiar crimson-orange colour. Three months after this another sister, aged 8, also fell ill with jaundice and vomiting; on the second day headache and restlessness appeared, on the third day she began to recover.

In an epidemic outbreak of jaundice amongst convicts reported by Carville there were 11 fatal cases out of 47 attacked; and in no fewer than half of the cases hæmorrhages occurred.

A further point of resemblance between such severe cases of jaundice and acute yellow atrophy is that in such epidemics the disease is *peculiarly fatal amongst pregnant and suckling women.* Thus in the *epidemic which occurred in* Martinique in 1858, reported by Gallot, the only severe cases occurred amongst pregnant women, of whom no fewer than 20 died after abortion.

Now, it is noteworthy, in the same relation, that amongst the 4[illegible] recent cases of acute yellow atrophy collected by myself, no fewer than 9 (all in pregnant women) are recorded by three observers, and all of them Australian; from districts where epidemic outbreaks of jaundice seem comparatively common (Broken Hill Proprietary). Two of these cases, carefully recorded by Creed and Scot-Skirving (1889), are especially worthy of note, inasmuch as they presented all the clinical features of acute yellow atrophy, including diminution of liver dulness, yet ended in recovery. In one leucin and tyrosin were present in the urine, in the other the symptoms included severe nervous phenomena, petechiæ over limbs and trunk, and coffee-ground vomiting. Both occurred in pregnant women about the eighth month (8 and 8½ respectively), and they occurred in the same neighbourhood. In each case there was premature delivery on the seventh day. The five cases reported by one observer (Hardie, 1890) are closely alike; all of them ended fatally. In three the liver was found diminished in size during life, the observation being confirmed after death (30, 30, and 32 oz.) In two the urine contained both leucin and tyrosin, in one leucin without tyrosin. Six cases, indeed, are recorded by Hardie; but one of these (the third) I have not included, as it appears to me of doubtful nature.

The resemblance between acute yellow atrophy of the liver and severe fatal cases of *icterus gravis* is thus exceedingly striking. It extends not only to the clinical features and course and morbid anatomy, but also to the occasional endemic characters of the former disease. The resemblance is so striking as to render it probable that, in the one as in the other, toxic influences or agencies are at work; this presumption is the stronger in *icterus gravis* on account of its comparatively frequent occurrence in endemic and even in epidemic form. Of what nature these toxins may be, whether miasmatic or bacterial, we know as yet nothing.

In arriving at this conclusion, which appears to be most in consonance with the facts, it is not necessary to press it so far as to assume that the toxic agencies are specifically the same, and different only in degree. On the contrary, acute yellow atrophy is probably a specific variety of *icterus gravis.* Its occasional occurrence in endemic form, as in the cases above described, undoubtedly lends much support to the view that toxic influences of specific nature play the most important part in its etiology.

Symptoms.—At the onset of the disease there is nothing in the features of the malady to distinguish it from an ordinary attack of jaundice. The disease is ushered in with the same symptoms—loss of appetite, malaise, nausea and vomiting, and epigastric discomfort, followed in the course of a day or two by the appearance of jaundice. The only feature that may possibly mark it off from a simple attack of jaundice is the occurrence of some rise of temperature at the outset. This stage lasts on an average some five to six days; but it varies considerably. During this time the physical signs are in no sense obvious. The tongue is coated, the bowels constipated; the pulse averages 60-70 beats per minute, the respiration is unaffected; and, beyond perhaps some slight degree of epigastric tenderness on pressure, nothing abnormal is presented by the abdomen. There are in addition the usual signs of jaundice, both in the skin and in the urine.

Suddenly a marked change occurs, ushered in usually by severe and repeated vomiting. In a few hours the patient passes into a condition of drowsiness and semi-consciousness, followed by great restlessness and delirium; occasionally he screams out loudly, or attempts to get out of bed, or even becomes maniacal. Simultaneously the jaundice assumes a deeper and more of a greenish hue, the tongue becomes dry and brown, the pulse rapidly rises in frequency (120-140) and loses in strength, the respiration is quickened. The temperature, which in the first stage may have been considerably raised, now becomes subnormal. The vomiting, hitherto perhaps intermittent, again recurs with greater severity than ever, it becomes almost continuous; the vomited matter frequently contains blood; blood may also be passed by the bowel, making the stools dark and offensive; hæmorrhages also occur under the skin or from the nose and mouth; in women severe metrorrhagia sets in, and in pregnant women abortion or premature delivery ensues.

The most notable physical change, however, is that presented by the liver, rapid diminution in the area of hepatic dulness, so that instead of the usual area from the fifth rib to the edge of the costal arch, it may be reduced to a finger's breadth; or in severe cases it may disappear altogether.

Next to the liver the most marked changes are presented by the urine. Contemporaneously with the changes in the liver the urea is diminished, and its place is taken by abnormal constituents—notably by tyrosin and leucin. Not infrequently also albumin is present, although only in small quantity.

The second stage, marked by the above severe symptoms, is of short duration. Under the combination of them all the patient rapidly passes into a muttering delirium, with or without *convulsions, and dies in* from two to three days.

If, passing from the above general description of the ordinary course of the disease, we consider the more prominent features in detail, the most notable, and that which gives the name to the disease, is undoubtedly the peculiar change in the liver.

The *diminution in the area of hepatic dulness* usually does not become manifest until after the onset of the severe nervous symptoms, and often not till within a few hours of death. Within this period of time it proceeds so rapidly that in the course of forty-eight hours the vertical dulness in the right mammary line may be reduced from the normal 5 or 6 inches to 1 or 1½ inch. The diminution first becomes manifest in the left lobe, and subsequently in the right. If the liver has been *previously enlarged from any cause, as by cirrhosis, fatty infiltration, gall-stones, or syphilis,* the diminution may be scarcely evident if at all; but, in uncomplicated cases, it is easily made out towards the end of life, all the more readily because of the absence of meteorism or any other abdominal distension. As subsequent examination shows, the diminished dulness is due partly to diminished volume of the organ, but also in part to a falling back of the flabby and greatly shrunken organ from the anterior abdominal wall.

As regards the condition of the liver in the earlier stages of the disease, observations are, unfortunately, but scanty, and for the most part those that exist are at variance. In the majority of cases the condition of the liver was not noted until the onset of the severe nervous symptoms directed attention to the true nature of the case. By this time the diminution in size has usually begun. In a certain number of cases, however, in which earlier observations had been made, the stage of diminution was found to have been preceded by one of enlargement. In one such case the hepatic dulness on the first examination was found normal; two days later it was increased; and two days later still it was reduced below the normal size.

In a case recently recorded by Sir Dyce Duckworth (1892), in a man aged 41, the liver dulness at the time of the first observation was found to extend from the 6th rib to just above the level of the umbilicus in the nipple line, the edge of the liver being palpable. On the following day the edge was no longer palpable; and two days later it had disappeared altogether over the back and axillary region, and in the nipple line it extended only 1½ inch downwards from the 6th rib. After death the liver was found to weigh 28 oz. (instead of the normal 50-60 oz.)

The position in which the remaining dulness is to be detected is usually, as in the above case, in the neighbourhood of the 6th rib, extending an interspace or a little more downwards.

In a case of a man, aged 28, who died in four days from the first onset of symptoms, and two days after he had been walking about, the liver dulness was reduced to 1½ inch below the 5th intercostal space; and in another case, a man aged 25, it extended from the 6th rib to the lower border of the 7th.

In a case of a woman aged 26, on the fourth day the area of hepatic dulness was only one inch deep; and on the next day it had disappeared altogether.

The diminution in area of dulness is usually the more marked, inasmuch as in general there is an entire absence of meteorism.

In but few cases is the liver dulness normal, and they are usually cases in which the liver has been chronically enlarged. Even in these, however, the dulness is reduced, although it does not fall below the normal.

As regards the frequency with which this change occurs, the records are unfortunately imperfect. Thus out of 44 recently recorded cases collected by myself, *in only 24 is mention made of the condition of the liver during life. In the great majority of these, shrinking was detected* (21 out of 24).

In some cases there is sensitiveness on pressure over the liver, sometimes to a very high degree; especially during the second stage. But this is not constant; more usually there is merely dull pain over epigastrium.

Gastro-intestinal symptoms.—The gastric symptoms are prominent in all cases; they include nausea, sickness, coated tongue, and above all vomiting. This is often met with in the first stage as one of the earliest symptoms; but it is a constant feature of the second stage, and is of a particularly urgent and severe character. The vomit soon tends to assume a dark colour from presence of altered blood, and resembles treacle in appearance; sometimes it contains bile.

The bowels are usually constipated, and may be so throughout; but in some cases, especially in the second stage, they are loose, and the motions very offensive. They often contain bile, and sometimes altered blood.

The jaundice is in the great majority of cases one of the earliest symptoms, making its appearance a few days after the first feelings of illness. At first it differs in no respect from that due to simple catarrh, the urine giving the usual Gmelin's reaction of bile pigment. It may vary somewhat in intensity during the first stage; but, as a rule, it steadily increases till the second stage, when, with the onset of the nervous symptoms, it suddenly deepens and at the same time alters in character, the discoloration of the skin assuming a greenish tint.

With this change there may also be a change in the character of the pigments in the urine. The urine may still be dark and give a yellowish foam, as if from much bile pigment; but, on testing, Gmelin's reaction may be faint or even entirely absent. Bile acids have been found in many cases.

In a few rare cases presenting all the features of the disease, including atrophy of the liver, jaundice has been absent, or has been confined to the liver. But these must be regarded as quite exceptional instances.

Fever.—A certain degree of fever is usually met with in the first stage at the outset; it then falls to normal or subnormal again, usually rising during the second stage. But there is no general rule.

In the first stage the temperature may be normal or even subnormal (96°); then, with the onset of nervous symptoms, it may rise to 102° or 103°, sometimes becoming hyperpyrexial just before death, attaining 105° to 106° F. (3 out of 16 recent cases). In other cases the temperature may never rise above 99° F.; or may remain persistently below the normal 96° to 98° F. (8 out of 16 cases). In other cases, again, the temperature may be high to begin with (103° F.), and then, with the onset of the second stage, fall below the normal (97·5° F.) (3 out of 16 cases). In other cases the temperature may not rise till the last twenty-four hours before death, when it may become hyperpyrexial (105° F.) (2 out of 16 cases).

Hæmorrhages are very common: they are met with in more than one-half of the cases.

Hæmatemesis is most common: melæna (one-fourth of the cases), petechiæ, and ecchymoses under skin, are not infrequent: less frequently *epistaxis occurs, and in a few cases hæmaturia; in women metrorrhagia is common.*

Hæmorrhages are a feature of the second stage.

The Urine.—The urine is usually slightly diminished in quantity, varying in specific gravity from 1015 to 1030; it is deeply bile-stained, and sometimes throws down a heavy deposit of urates. It usually gives a well-marked reaction to Gmelin's test for bile pigments. But other pigments are obviously present; for sometimes, notwithstanding bilious colour, this reaction is not given. It is probable that urobilin is greatly increased in such cases; but on this point information is much required. In one recent case indican was much increased.

Albumin is often present, but seldom in any quantity. Out of 24 recent cases in which the urine was examined, in only one was much albumin present.

Sugar is not found.

Urea is usually much reduced—sometimes to a mere trace; that it should be greatly reduced is not at all surprising when we consider that in health the amount excreted depends mainly on the quantity of food taken; and that, in the second stage of this disease, owing to the constant vomiting, no food is retained. Information is greatly wanted as to the extent of the reduction met with. Among recent cases, 44 in number, there are only 24 in which information as to urine is forthcoming; and out of these 24 I find only 7 in which the urea was estimated.

In a case recorded by Dr. Cayley, the urine four days before death was found to contain only 0·7 per cent of urea, instead of the normal 2 per cent. Neither leucin nor tyrosin was present. The liver weighed 33 oz.

In a case recorded by Dr. Cullingworth, in which the urine was investigated by Professor Gamgee, the amount of urea in twenty-four hours was 6·67 grammes instead of the normal 30 grammes. In this case there was no trace either of leucin or tyrosin in the urine, although these substances were present in the liver. The liver weighed 24 oz. (the normal weight being about 50 oz.)

In a case recorded by Dr. Ralfe the percentage of urea was 1·9; leucin and tyrosin were present. The liver weighed 34 oz. He refers to another case observed by him in which the urea was but slightly diminished.

In a case recorded by Sir Dyce Duckworth the percentage of urea, on the day before death, was found to be 1·6, and next day 1·5. The liver weighed 28 oz. On the first examination tyrosin was found, with doubtful leucin ; in the last neither leucin nor tyrosin was present.

Leucin and Tyrosin.—The presence of these bodies constitutes the most characteristic feature of the urine in this disease. The latter is sometimes thrown down in crystals on cooling; the former appears on evaporation of the urine. Frerichs found them in every case in which he looked for them; later observations, however, show they are by no means constantly present.

Out of 34 cases collected by Thierfelder, in which the urine was examined in this relation, in 7 the result was negative ; in 17 both were found ; in 3 tyrosin only ; in 7 leucin only.

Out of 23 recent cases collected by myself, in 9 neither was found ; in 10 both were found ; in 3 tyrosin only ; in 1 leucin only.

In one of the cases in which neither was found (Gamgee), it is interesting to note that both were found in the liver; as much as 10 grains of leucin and over half a grain of tyrosin were found.

Duration.—The duration of the disease from start to finish varies considerably, according as it attacks one previously healthy, or supervenes on some other affection of liver. In the majority of cases it does not exceed 14 days, and rarely does it exceed three weeks.

Duration of Disease.

THIERFELDER. 102 Cases.			HUNTER. 29 Cases		
Days.	Cases		Days	Cases	
2– 4	5	54	2– 4	4	15
5– 7	18		5– 7	3	
8–14	31		8–14	8	
15–21	22		15–21	5	
3– 8 weeks.	26		3– 8 weeks.	9	

Among recent cases collected by me, in only one did it exceed 31 days, namely, 57 days (Glynn).

The relative duration of the two stages of the disease varies within wide limits.

In certain cases, indeed, where the disease supervenes on some other morbid condition of liver, such as cirrhosis, it is not possible to determine when the disease commences.

First stage.—In 24 recent cases in which information on this point is forthcoming, the duration of the first stage, from the first onset of symptoms to the appearance of the nervous disturbances ushering in the second, varied from two days to three or four weeks. In two cases it exceeded four weeks ; namely, over six weeks (Cayley), two months (Glynn).

Second stage.—Of greater interest is it to ascertain the duration of the second stage, when the true nature of the disease is recognised.

Thus in 26 of my cases, in which information on that point is given, I find the duration of the second stage varied from one to seven days, and on an average was from two to three days.

Duration of Second Stage in twenty-six Cases.

Days	Cases.
1–2	12
3–4	12
5–7	2

These results agree with those of Thierfelder, obtained from 118 cases; namely:—

Days	Cases
1– 2	56
3– 4	43
5– 7	15
9–14	4

According to their severity it has been proposed by Thierfelder to divide cases into three groups: peracute, subacute, and protracted. It appears, however, hardly worth while to distinguish relative degrees of acuteness in a disease which, once it has manifested itself, is usually so acute. The disease, however, is not invariably fatal. A considerable number of cases are now recorded in which recovery has taken place. Two such cases are recorded by Creed and Scot-Skirving. The first was that of a woman aged 24, in the 8th month of pregnancy, who was attacked with severe jaundice, and was delivered spontaneously on the 7th day. Hepatic dulness was greatly lessened, and leucin and tyrosin were found in the urine. She recovered in the course of six weeks, the area of hepatic dulness being then found normal.

The second case was that of a woman aged 23, between the 8th and 9th months of pregnancy. She suffered from moderate jaundice lasting a week, and then urgent symptoms set in—including coffee-ground vomiting and petechiæ on limbs and trunk—and she was delivered prematurely of a jaundiced child on the 7th day. The extent of liver dulness was reduced to three fingers' breadth. In this case no leucin or tyrosin was discovered in urine.

Morbid anatomy.—The chief change is presented by the *liver*. This is greatly reduced in size, and is found lying collapsed, with smooth surface and wrinkled capsule, fallen away from the ribs in the right hypochondrium. Both on surface and on section it shows a number of orange-yellow patches of varying size and irregular outline, distributed irregularly throughout its substance; the remainder of the liver is of reddish colour, of uniformly soft consistence, and its lobules much smaller than normal. In the yellow portions the lobules cannot be distinguished.

On microscopic examination the liver-cells are found extensively degenerated; they are swollen with indistinct nuclei, and the cells are filled with fat granules. In parts they have entirely disappeared, and are represented by masses of fat granules held together by the liver stroma.

The appearances differ somewhat in the yellow and red portions. In the latter, in addition to fatty degeneration, there is in some cases a small-celled infiltration around the portal vessels and throughout the lobule; the interlobular bile-ducts being numerous and prominent, their epithelium tinged with bile, and their lumen filled up with small masses of bile pigment. The larger bile-ducts are usually free from bile, and contain mucus only; but the gall-bladder often contains some bile.

The reduction in size is variable, but amounts on an average to one-third or more. Among forty-four cases collected by me the weight of the liver is given in twenty-eight cases occurring in adults. In five of these the weight was below 30 oz. (the average normal weight being 50 oz.); namely, 24, 25, 23, 23, and 28 (Cullingworth, Suckling, Tomkins and Dreschfeld, Moore, Duckworth, respectively). In nineteen the weight varied between 30 and 38 oz. In one the liver was enlarged—66 oz.—from old-standing fatty disease (Dreschfeld). *Leucin and tyrosin* have been found in the liver in a considerable number of cases: out of thirty-four cases examined in this respect, in fourteen both were found; in six, leucin alone; in four, tyrosin only; in twelve, neither substance (Thierfelder). Among recent cases only three appear to have been examined in this respect; in two both substances were found (Cullingworth, Pincherle); in the other neither was found (Suckling). Dr. Cullingworth's case is of special interest, as one of the most fully investigated cases on record (1881); the histological investigation was carried out by Professor Dreschfeld, and the chemical investigation by Professor Gamgee, who determined the actual amount of leucin and tyrosin in the liver; namely, 10·8 grains of leucin, and 0·56 grains of tyrosin. Curiously enough, no trace of these bodies was found in the urine

Micro-organisms have been sought for in a few cases, but usually with negative results. Bacteria and micrococci have been described by Klebs in three cases; they were present in the large and small bile-ducts, as well as in the interstitial connective tissue. Among recent cases three have been carefully examined by Dreschfeld (1881); in two of these the result was negative. Koch's method for detection of micro-organisms was applied to numerous sections with negative result. In a third case (that of Tomkins), examined half an hour after death, numerous large micrococci were found in the portal canals filling the arteries and capillaries; sparingly distributed in the yellowish portions, but more numerous in the reddish portions, chiefly in the peripheral part of the lobules and interlobular spaces: they were found only in those parts of the lobules where the liver-cells were either intact or only beginning to be diseased.

The *spleen* is usually more or less enlarged, soft, and diffluent; and sometimes this enlargement is recognisable during life. Among recent cases collected by me I find the weight recorded in six only; it varied from 5 *to 10 oz.: in two it is stated to have been enlarged; in other two it is stated to have been not enlarged.*

The *kidneys* show fatty degeneration of the epithelium of the convoluted tubules.

Hæmorrhages are present not only under the skin, but scattered throughout the mesentery, the pericardiac and pleural surfaces, the mucous membrane of stomach, the pelvis of kidney and the bladder.

Pathogeny.—The nature of this rarest of diseases is still for the most part wrapt in mystery. It may be (i.) a general constitutional disease to which the atrophy of the liver is only secondary; or (ii.) a primary disease of the liver—an acute inflammation leading to destruction of the secreting structure; or (iii.) a form of phosphorus poisoning; or (iv.) a rare form of infective disease, having its relations, not with constitutional disease, but with other forms of jaundice produced by infective agents.

(i.) In favour of the first proposition, it has been pointed out that not the liver only, but other organs—the kidneys and the heart—are also found fattily degenerated.

(ii.) In favour of the second proposition, it is pointed out that the changes are undoubtedly most marked in the liver; and that the more characteristic symptoms of the disease appear to be directly related to the liver changes rather than to those in any other organ.

Are the liver changes of an inflammatory nature, or only degenerative? In favour of their inflammatory character a small-celled infiltration in and around the lobules is pointed out by several observers; this, however, has been found in a few cases only, and limited to the red portions. The degeneration is often as marked in the yellow where there is no evidence of inflammation.

(iii.) In favour of its being a variety of phosphorus poisoning is that in phosphorus poisoning, as in acute yellow atrophy, fatty degeneration of the liver is the chief morbid change, and that the symptoms of the two conditions are closely alike, even to the appearance of leucin and tyrosin in the urine.

(iv.) Lastly, in favour of the fourth alternative—that we are dealing with a rare form of infective disease—is the fact, already pointed out in discussing the etiology of the disease, that cases indistinguishable from acute yellow atrophy of the liver have been met with during outbreaks of severe epidemic jaundice; and that generally the symptoms and course of the disease, even in the minutest particulars, are practically the same as those met with in the severest forms of what is termed "malignant jaundice." Thus among recent cases I find no fewer than nine recorded by three observers in Australia, from districts where cases of infective jaundice are common.

An extensive epidemic outbreak of jaundice which occurred in Saxony and Dresden in the autumn of 1889 has been recorded by Meinert; no fewer than 518 persons were attacked. There were two stages in the disease: an initial febrile stage with rigor, sickness, headache, but without jaundice; and a second stage of jaundice without fever, the fever falling on the second or third day, and the jaundice appearing on the fifth or sixth day, and lasting on an average about eleven days. Of these cases thirteen died, and two of these with all the symptoms of acute yellow atrophy.

The evidence in favour of acute yellow atrophy being a rare form of malignant jaundice of obscure infective nature appears to me far to outweigh that in favour of any other of the propositions I have cited.

The resemblance between the disease and phosphorus poisoning is important, in that it shows that certain poisons do possess the power of producing degeneration of the liver with profound disturbances of its metabolic functions, such as we meet with in acute yellow atrophy. But this resemblance is by no means so close as to justify the proposition that acute yellow atrophy is but an obscure form of phosphorus poisoning. On the contrary, there are many important points of difference between the two conditions. In the first place, we are apt to forget that, although in both there is a fatty degeneration of the liver, in phosphorus poisoning this change is, in the great majority of cases, attended by enlargement of the liver, not by atrophy. It is this atrophy, indeed, which constitutes the special feature of the disease before us; and herein it differs not only from phosphorus poisoning, but from other forms of jaundice due to poisons; as also from other forms of severe jaundice occurring in disease—the usual result in such cases being swelling and enlargement of the liver. Thus I always found toluylendiamin, which may be regarded as the most intense icterogenetic poison we are acquainted with, produce marked swelling of liver and of the spleen (in dogs). So also in the jaundice of yellow fever, of malarial fever, and of Weil's disease, enlargement of the liver is the rule.

It has been suggested that the size of the liver depends upon the length of time the disease has lasted; that the liver is large if the disease ends early, and small if the disease lasts long. The facts, however, in my opinion lend no support to this view. Even in the bodies of patients who have died four days after being apparently in perfect health, the liver has been found much reduced.

Thus in a case recorded by Dr. Church the total duration of the disease from start to finish was only five days, the second stage lasting only twenty-four hours: the liver was found reduced to 32 oz.

The atrophy of the liver is in my opinion one of the most characteristic features of the disease. On the other hand, a certain degree of enlargement, or at any rate no notable reduction, is no less a characteristic feature of phosphorus poisoning.

Although fatty degeneration occurs in both, yet in phosphorus poisoning it appears, in its earlier stages at least, to have invariably the character of a fat infiltration; whereas in acute yellow atrophy the change appears to be a necrobiotic one from the outset: the cell breaks down into fatty detritus at once.

Chemical analysis confirms this difference in the character of the *changes in the two diseases.* As I have pointed out (see the article on "Phosphorus Poisoning"), the percentage of fat in the liver of phosphorus poisoning is very greatly increased—some tenfold—from 3 to 30 per cent; while in acute yellow atrophy it is only slightly increased to 4 or 5 per cent.

While, then, the resemblances between phosphorus poisoning and acute yellow atrophy are so close as to lead us to suppose that in the latter case, as in the former, we are dealing with the action of a severe poison, there are nevertheless differences between the two which appear to indicate clearly that the poison is not the same in both cases.

On the other hand, the resemblances between acute yellow atrophy and the severest cases of malignant jaundice are even closer, and extend likewise to the production of degeneration of the liver-cells and to destruction of their functions; as evidenced by the occasional appearance of such products as leucin, tyrosin, peptones, and the like in the urine. Yet here again there are certain differences—notably the essentially degenerative character of the liver change in acute yellow atrophy—which appear to me to indicate that the poison is not the same in both diseases It can hardly be doubted, however, that it is of the same character; in both we have to do with a virulent organic poison probably formed within the intestine, and acting on the liver (as also on the blood and kidneys and other tissues) after absorption. It is possible that in certain cases this may be followed by an actual invasion of the liver by the organisms themselves, as in Professor Dreschfeld's case, where he found micrococci in the vessels and capillaries of the liver half an hour after death. But it is probable that such an invasion is not essential; that the absence of organisms, as in the two other cases examined by the same observer, is the more common condition. The widespread character of the liver change, and the rapidity with which it usually occurs, both suggest the action of a circulating toxin rather than a local invasion by micro-organisms.

As to the nature of the infection, the extreme rarity of the disease indicates that it must be of altogether exceptional origin. The comparative rarity of ordinary epidemic (catarrhal) jaundice strongly suggests, as it appears to me, that in this case we have to do with a "mixed infection." And the fact that the severest cases of this kind so strongly resemble acute yellow atrophy—in the mode of onset; in the character of symptoms, in the appearance of leucin and tyrosin in the urine; in the changes in the liver, including even diminution in size, and in the course of the train of symptoms—appears to suggest that in acute yellow atrophy we are also dealing with an exceptionally rare form of mixed infection.

Nature of the jaundice.—No obstruction is to be found in the larger bile-ducts; and the jaundice has long been regarded as a striking example of jaundice independent of obstruction. It has been variously ascribed to suppression of liver function, to hæmatogenous origin of bile pigment, to paralysis of bile-ducts, and to spasm of bile-ducts; in its production nervous disorder has been thought to play an important part (Liebermeister); and, finally, it has been ascribed to poisoning with biliary acids.

These surmises may, one and all, be regarded as no longer tenable, for reasons which I have fully discussed elsewhere. Bile pigments are not preformed in the blood; and at the time the jaundice appears there is no evidence of suppression of biliary function. On the contrary, even to the very last, bile continues to be formed; sometimes, indeed, there is actual polycholia during the second stage. In the majority of cases bile is to be found in the gall-bladder, sometimes in normal amount.

Although the larger bile-ducts are unobstructed, and usually contain only colourless mucus, the same does not apply to the smaller intra-hepatic bile-ducts. These, on the contrary, are found bile-stained, and usually filled by desquamated and fatty epithelium. The condition presented is, in fact, precisely the same as that found after poisoning with toluylendiamin or phosphorus; larger bile-ducts free from bile; smaller bile-ducts filled with inspissated bile, due to obstruction high up. The jaundice is due to catarrh, going on subsequently to complete fatty degeneration of the epithelial lining of the finest bile-ducts.

The striking resemblance between the disease and that producible by poisons leaves, in my view, no room for doubt, that in it we have to do with that variety of catarrh of the bile-ducts which I have called "toxæmic"—that is, a catarrh produced by the excretion through the bile of the injurious products which cause extensive degenerative changes in the liver-cells.

The view, originally put forth by Buhl (1854), that the cause of the jaundice is mechanical obstruction of the smallest bile-ducts by degenerated epithelium, a view subsequently supported by Bamberger and Cornil, has thus received strong confirmation.

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REFERENCES

1880-1886.—3. Armitage, J. *St. Bart. Hosp. Rep.* 1881, p. 264.—4. Bowen, J. *Arch. Med. N. Y.* 1884, 175-179 —5. Carrington, R. E. *Trans. Path. Soc.* 1884-5, vol. xxxvi.—6. Cavafy, J. *Ibid.* 1882-3, vol. xxxiv p. 122.—7. Cayley. *Brit. Med. Journ.* 1883, i p. 623.—8. Chew, S. C. (With P.M. exam.) *N. Y. Med. Rec.* 1883, xxiv. p. 369 —9. Church. *Brit. Med. Journ.* 1884, i. —10. Clubbe, C. P. B. *Lancet*, 1883, ii. p. 96.—11. Cullingworth. *Med. Times and Gaz.* 1881, ii. pp. 263, 291.—12. Dreschfeld. (Morbid Histology.) *Jr. Anat. and Physiol.* 1880-81, xv. 422-430.—13 Glynn. *Liverpool Med -Chir. Journ.* 1882, ii. p. 364.—14. Goodhart. (A child aged 2.) *Trans. Path. Soc.* 1881-2, xxxiii. p. 170.—15. Van Haren Noman. *Arch. f. path. Anat.* 1883, Bd. xci. p. 334.—16. Hlava. *Prag. med. Woch.* 1882, vii. p. 421.—17. Jones, H. (In a young man.) *Med. Times and Gaz.* 1880, i. p. 477. —18. Kahler. *Prag. med. Wochenschr.* 1885, x. p. 213.—19. Le Roy, G. *Lancet*, 1885, ii. p. 155.—19*a*. Legg, Wickham. *Bile, Jaundice, and Bilious Diseases*, 1880.—20. Loomis, A. L. *New York Med. Journ.* 1880, xxxi. p. 31.—21. M'Dowall, J. W. Following rotheln (?) in a melancholiac (with temp. chart). *Jour. Ment Soc* 1881-2, xxvii. p. 541.—22. Mader. *Wien. med Bl.* 1885, viii. p. 294.—23. Marsh, E. F. *New York Med. Rec.* 1885, xxvii. p 203.—24. Musser, J. H. *Phil. Med. Times*, 1882-3, xiii. p. 43; *Amer. Journ. Med. Soc.* 1884-88, p. 166.—25. OSSIKOVSZKY. (Identity with Phosphorus Poisoning.) *Wien. med. Woch.* 1881, xxxi. p. 937.—26. PINCHERLE. (A case.) *Wien. med. Woch* 1886, xxxvi. p. 1022.—27. RALFE. *Lancet*, 1881, i. p. 780.—28. SALKOWSKI. (Chemistry of the subject.) *Virch. Archiv*, lxxxviii. 1882, p. 394.—29. SUCKLING. *Brit. Med. Journ.* 1884, i. p. 358.—29*a*. THIERFELDER. *Ziemssen's Cyclopædia*, ix. 1880.—30. TOMKINS. *B.M.J.* 1883, i. p. 818, *Lancet*, 1884, i. p. 606.—31. VENN. *Lancet*, 1884, ii. p. 191.

1887.—32. MOORE. (2 cases.) *Austral. Med. Jour.* 1886, viii. p. 446.—33. JOHNSON, C. W. *Brit. Med. Journ.* 1886, ii. p. 1031.—34 REDTENBACHER. (A case.) *Wien. med. Bl.* 1886, ix. p. 1439.—35. ELSNER. *Austral. Med. Gaz.* 1886-87, vi. p. 224.—36 HOLT, A. F. *Boston Med. and Surg. Journ.* 1887, cxvii. p. 374.

1888.—37. ROSS, J. C. *Lancet*, 1888, i. p. 972.—38 APPLEYARD. *Med. Press. and Cir.* 1888, xlv. 659.—39. ROHMANN. (Chemistry of the subject.) *Berl. klin. Woch.* 1888, 861.

1889.—40. BARR. *Med. News, Philad.* 1889, liv. 540.—41. ROSENHEIM. *Zeit. f. klin. Med.* 1888-89, xv. p. 441.—42. FOLTANEK. *Wien. klin. Woch.* 1889, ii. p. 294.—43 CREED and SCOT-SKIRVING. (2 cases with recovery.) *Austral. Med. Gaz.* 1888-89 viii. p. 259.—44. HAYWARD. *Ibid.* 1889-90, ix p. 17.

1890.—45. BUSS. *Berl. klin. Woch.* 1889, xxvi. p. 977.—46. MADER. (Without atrophy of liver or jaundice) *Ber der k. k. Krank. zu Wien.* 1889, 387.—47 SCHICKHARDT. *Munch. med. Woch.* 1889, xxxvi. 756.—48. DORFLER. (Etiology.) *Munch. med. Woch.* 1889, xxxvii. 878.—49. HARDIE. (In pregnancy.) *Austral Med. Gaz.* 1889-90, ix. p. 179.—50. MUELLER. *Ibid.* 211.

1892.—51. DUCKWORTH. *Lancet*, 1892, i. p. 630.—52 YEOMAN. *Lancet*, 1892, ii. p. 422.—53. GAIRDNER and COATS. *Glas Med. Journ.* 1892, xxxviii. 287.—54. NEINERT. *Centralb. f. klin. Med.* 1891, p. 270.

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PERIHEPATITIS

BY this name we understand an inflammation of the peritoneal capsule of the liver. It may be acute or chronic, but the acute form, being but an unimportant part of some other acute process, such as acute peritonitis, hepatic abscess, or acute pleurisy, is of little interest.

Chronic perihepatitis is either universal—over the whole liver, or scattered in patches on its surface; in the latter case it is usually called **local perihepatitis.** This variety has many causes which will readily suggest themselves to the reader; as instances, I may mention the local peritonitis over the liver which is merely part of a tubercular or cancerous peritonitis; that which is seen around the gall-bladder in some cases of gall-stones; the thickening of the hepatic capsule seen in the neighbourhood of a gastric ulcer which has become adherent to the liver; the local peritonitis which may occur over a hepatic cancer, and the local peritonitis which radiates from a gumma or a syphilitic scarred depression on the surface of the liver. Local perihepatitis occurring in patches is very common when there is marked backward pressure in pulmonary or cardiac disease; among eighteen examples of it, in ten there was either cardiac or pulmonary disease. Capsulitis of the spleen is very commonly associated with local perihepatitis. Probably it hardly ever becomes universal.

The thickened capsule cannot readily be peeled from the surface of the liver, save in quite exceptional cases; and it commonly shows several little pits on its surface, which give it a meshed appearance. Usually no symptoms can be detected, but a rub can occasionally be felt or heard over the liver; and perhaps local perihepatitis may sometimes explain the hepatic pain of which sufferers from diseases of the heart and lungs, or cirrhosis of the liver, often complain.

General or universal perihepatitis is a very different condition; in it the whole capsule becomes thick, opaque and white. This white jacket, which may be a quarter of an inch thick, easily peels off the subjacent liver, the surface of which is smooth; and for some unexplained reason it is quite common to find the inferior edge of the liver folded up on to the anterior surface of the organ. Fagge mentions a case in which the lower margin of the liver touched a point on the anterior surface that should have been 4½ inches distant from it. As a result of the folding, the lower edge of the liver cannot be felt at all; and, if the liver can be made out by tactile examination, the surface, at first taken for the lower edge, feels particularly thick and rounded. The upper and lower folds of peritoneum which form the posterior ligament of the liver become so thick that they are approximated. Often little pits are to be seen on the surface of the thickened capsule. Occasionally the early stage of perihepatitis is met with in the post-mortem room, in patients who have died of some other affection; then the liver is simply covered with a thin layer of white lymph which easily peels off.

Writers express different opinions upon the condition of the liver in universal perihepatitis. Murchison states that perihepatitis leads to atrophy of the liver, and that "fibrous bands also pass from the thickened capsule into the interior of the liver, which on section presents a dense, smooth, uniform surface with the outline of the lobules more or less obliterated"; but, as he goes on to say that this is especially seen in syphilis and long-standing backward pressure from heart disease, there is, I think, little doubt that he is describing extreme cases of the patchy perihepatitis to which I have just alluded. Fagge, on the other hand, says the hepatic "tissue is commonly soft, and is very often loaded with fat. It is seldom cirrhotic, but there is sometimes an excess of white fibrous tissue in the course of the large portal vessels." This description certainly agrees with what I have observed for myself; and among twenty-two consecutive cases of universal perihepatitis that have occurred at Guy's Hospital I find the liver was never markedly cirrhotic; its tissue was nearly always soft. In two instances in which the patient had had syphilis it was lardaceous; and in some cases where in the heart or lungs there was any cause for increased venous pressure it presented the nutmeg appearance.

The liver with its thickened capsule generally weighs about the same as a healthy liver; from this we may conclude that the organ is a little atrophied. The thickened capsule hardly ever exercises sufficient pressure in the transverse fissure to compress the bile-duct; jaundice is extremely rare in perihepatitis, and I never heard of the gall-bladder being dilated.

Many authors assume that, as ascites is very common in perihepatitis, the flow through the portal vein is impeded either by the pressure of the thickened capsule on the portal vein in the transverse fissure, or by its pressure on the liver as a whole; but *against this view stands the fact that jaundice is so rare, and it is difficult to believe that the increased pressure would always fall upon the portal system and never on the bile-ducts.* Then, again, in a case of perihepatitis in which the ascites had been so severe that, at various times, nearly 800 pints of fluid had been withdrawn from the abdomen, I carefully dissected the portal vein, and could not find any evidence that it was dilated; or that it was constricted by the thickened capsule of the liver as it passed through it at the transverse fissure of the liver.

The consideration of pressure on the portal vein naturally leads us to that of the conditions associated with perihepatitis; for I shall show that this universal perihepatitis, as it is almost always associated with a chronic general peritonitis, should be regarded merely as a part of it; in this fact we have an explanation of the frequency of ascites and the rarity of jaundice. I took quite indiscriminately from the post-mortem records at Guy's Hospital forty consecutive cases of perihepatitis; eighteen were examples of partial and twenty-two of universal perihepatitis. Of the eighteen cases six were instances of peritonitis due either to tubercle or cancer, and the thickening of the capsule of the liver appeared to be merely part of the general peritonitis; of the remaining twelve only one is stated to have had peritonitis, and, of the eleven left, eight are distinctly stated not to have had any peritonitis; in the remaining three the peritoneum is not mentioned. Turning now to the twenty-two cases of universal perihepatitis, in only two is it stated that there was no peritonitis; in seventeen it is distinctly stated that there was peritonitis, and in the remaining three no mention is made of the peritoneum. The peritonitis was always chronic, and was never due to tubercle or growth; it was always of that well-known variety in which the peritoneum becomes thickened and opaque; the omentum is puckered up towards the colon, where it forms a transverse ridge often mistaken for the lower margin of the liver; the mesentery becomes shortened so that the intestines are dragged back to the spine, and in an extreme case they may become so matted together that they can be removed as one mass, from which it may take an hour to dissect them: they may even be puckered up parallel to their long axis, so that the distance from the duodenum to the cæcum is much lessened. Sometimes the material which mats the intestines together can be stripped off, leaving their smooth serous surface exposed; and thus we see the similarity between this chronic peritonitis and universal perihepatitis.

Ascites is a very frequent symptom of simple chronic peritonitis, and I would argue that, as we have just seen, constriction in the portal venous system being improbable, we ought to regard the ascites which accompanies perihepatitis as the result of the associated chronic peritonitis. This view is strongly supported by the fact that in the only two cases I have come across in which universal perihepatitis occurred without chronic peritonitis there was no ascites.

In the twenty-two cases of universal perihepatitis, capsulitis of the spleen was stated to be found in fourteen, and in only two was it said to be absent. It was always universal, and should, like the perihepatitis, be looked upon merely as part of the general chronic peritonitis. By far the most important association is that in nineteen of the twenty-two cases the kidneys were granular. There seems but little doubt that universal perihepatitis should usually be regarded as a sequel of interstitial nephritis, for it is well known that the chronic peritonitis of which it is a part is a complication of this disease. As might be expected, in several of the nineteen there was some evidence of failure of the heart or lungs, and consequently sometimes the liver was nutmeg; in one case in which the cardiac failure was very marked there was jaundice, but this was the only instance of jaundice in perihepatitis. In four cases there was gout; in one more it was doubtfully present; in two others there was a strong family history of it; and in six cases there was a history of alcoholic excess: but it is particularly noteworthy that in none of these cases was there any marked cirrhosis,—in fact, in many of them it is distinctly stated that the liver was soft. In three instances syphilis was a very prominent feature in the case, and this disease was probably the cause of the perihepatitis in those two patients in whom no chronic peritonitis was present.

The average age at death in the cases of universal perihepatitis was 47½ years; the youngest was 29, the eldest 68. The proportion of males to females was as 13 to 8.

The symptoms of universal perihepatitis need not detain us long. In the first place, we nearly always find albuminuria and other evidence of chronic interstitial nephritis; secondly, the liver is rarely enlarged, and the edge, if it can be detected at all, is thick, uniform, and felt just under the ribs; thirdly, there are the signs of chronic peritonitis, the most conspicuous being the formation of an elongated tumour lying transversely across the abdomen above the umbilicus distinct from the edge of the liver, and made of the thickened puckered omentum; perhaps also other peritoneal thickenings may be felt in other parts of the abdomen. The accumulation of ascitic fluid quickly makes the abdomen dull to percussion, even at the umbilicus, if the shortening of the mesentery draws the intestines back to the spine. The ascitic fluid is sometimes loculated between the matted intestines, and then the diagnosis may be very difficult; but commonly it presents the ordinary signs of ascites, and it is particularly characteristic of it that it re-accumulates quickly after paracentesis: thus the abdomen may be tapped several times, usually three or four times, before the patient dies from exhaustion. A remarkable case was under my care eight years ago in Guy's Hospital. The patient was a sailor who had had syphilis; from 25th December 1885 to 4th August 1887 he was tapped thirty-five times, and the total amount of fluid withdrawn was 790 pints; the largest quantity taken out at any time was 31½ pints, and the average was about 23 pints. He ultimately sank and died in August 1887, and was found to have perihepatitis, chronic peritonitis, interstitial nephritis, and general lardaceous disease. As is usually the case, the fluid was clear and straw-coloured.

The common diagnostic difficulty at the bedside is to distinguish *between perihepatitis and cirrhosis with ascites. If jaundice be present the patient almost certainly has cirrhosis; if the signs of chronic peri-*tonitis or those of interstitial nephritis are well marked, the presumption is much in favour of perihepatitis; but both chronic peritonitis and interstitial nephritis may be associated with cirrhosis. The main distinction lies in this, that in cirrhosis the ascitic fluid generally collects quickly, and the supervention of ascites—at any rate in sufficient quantity to require tapping—almost always means that the end is not far off; so that in cirrhosis the patient rarely lives long enough after the first tapping for a second to be necessary, while in chronic peritonitis with perihepatitis he does not usually sink till after the abdomen has been tapped two or three times or oftener. I have published a series of thirty-four cases illustrating these points. Ten suffered from cirrhosis with ascites and died before tapping was necessary; they show very well how the supervention of ascites in cirrhosis heralds death, for the average duration of life after the abdomen was first noticed to be enlarging was only eight weeks. There were fourteen undoubted cases of cirrhosis in which paracentesis was performed. Here also the average duration of life after the abdomen was first noticed to be enlarging was eight weeks; in some of the cases the patient was dead within a month, and in only two was life prolonged beyond three months: in not one did the patient survive the first tapping long enough for a second tapping to be necessary, and in not one was there any evidence that the tapping was beneficial. The remaining ten of my cases were those which were regarded during life as having cirrhosis, but were tapped oftener than once; of these, in four the post-mortem examination proved the diagnosis to be wrong, one turning out to be a case of colloid disease of the peritoneum, and each of the other three had chronic peritonitis and perihepatitis: the remaining six had peritonitis more or less chronic associated with the cirrhosis.

Since I collected these cases I have seen two undoubted cases of uncomplicated cirrhosis in which life continued long enough to render a second paracentesis necessary; but I have also seen several cases, diagnosed as cirrhosis, which had been tapped several times, but in which it was found that the diagnosis was incorrect; for they had no cirrhosis, but chronic peritonitis with perihepatitis. Cirrhosis of the liver is often found in persons who have died from accident or from some disease which is quite unconnected with the liver; but it seems to me that all persons with cirrhosis, although for years it may produce no symptoms, are liable at any time to the rapid development of symptoms which quickly increase in severity, and show that life will soon come to an end. The chief of them are ascites, jaundice, a general feeling of illness, drowsiness, and swelling of the feet. Chronic peritonitis and perihepatitis, on the other hand, are very rarely found in those dead of diseases other than interstitial nephritis, of which it is a complication; from this, as Fagge observed, we may infer that it is a progressive condition, and one which is ultimately fatal. He states there is one fatal case of ascites from perihepatitis to every five fatal cases of ascites from cirrhosis [*vide* art. "Cirrhosis," p. 177].

Treatment is of little avail. Paracentesis must be performed when necessary; perhaps iodide of potassium is the best drug to use. In one case I tried leaving a tube for some time in the abdominal cavity to let the fluid run out as it formed, but this method did not prove of any benefit.

W. Hale White.

REFERENCES

Fagge. *Guy's Hospital Reports*, vol. xxxv pp 196, 202 - Murchison. *Diseases of Liver*, 2nd edition.—White, W. Hale. *Guy's Hospital Reports*, vol. xlix.

SUPPURATIVE HEPATITIS

Suppurative hepatitis presents itself under four forms: (I.) *Pyæmic hepatitis*, occurring as part of a general infective process in which the liver, along with other organs, becomes the seat of metastatic abscesses; (II.) *Portal pyæmia*, in which the pyæmic process resulting in multiple metastatic deposits has its point of departure in the portal tract, and is limited, as a rule, to the liver, which acts as a barrier to the passage of the pyogenetic micro-organisms into the general circulation; (III.) *Pyosepticæmic multiple abscesses*, following the spontaneous or surgical opening of tropical liver abscess, due to the introduction of septic organisms into the abscess cavity; (IV.) *Tropical or endemic hepatitis*, restricted mostly to tropical or subtropical countries, associated with or independent of dysentery, giving rise to one or several large abscesses, and (V.) *Cholangitis* (*vide* p. 257).

In the pyæmic forms we have to do with abscesses in the liver; in the tropical form with abscess of the liver. The liver, at the outset, is presumably sound in pyæmia; or, if diseased, this fact has nothing to do with the process or its results. In tropical hepatitis, on the other hand, the nutritive and functional condition of the organ is always more or less impaired; hence a diminution of its disease-resisting power, which is an important factor in the evolution of the abscess. The pyæmic and pyosepticæmic forms are common to all latitudes, while endemic hepatitis is above all other diseases, dysentery not excepted, a malady peculiar to warm climates.

It has been lately shown that suppurative hepatitis in warm climates is not infrequently a complication of amœbic dysentery, and that amœbæ are also found in a certain number of cases of liver abscess in which dysentery is absent. Whether the amœbæ in either case are the direct agents of suppuration, or simply act as the bearers of pyogenetic bacteria has not been finally settled; nor have we the means of deciding with any degree of precision to what extent tropical liver abscess is of amœbic origin. It appears probable that most cases of the so-called idiopathic liver abscess, *and perhaps a majority of those associated with dysentery, are not of the amœbic variety, but directly dependent on the presence of the ordinary micro-organisms of suppuration.* The amœbic form of liver abscess is treated of elsewhere (p. 153), but in the sequel I shall take a general view of the etiology and pathology of tropical suppurative hepatitis, whether associated with dysentery or independent of it.

I. PYÆMIC LIVER ABSCESS.—**Etiology.**—The etiology of this form of suppurative hepatitis resolves itself into that of pyæmia. A wound is invaded by pyogenetic micro-organisms; the veins involved in the primary lesion are frequently, but not always, thickened, ulcerated, or occupied by adherent and more or less decomposed coagula. Minute infective particles, or fine zooglœa masses, find their way into the systemic circulation, become arrested in the hepatic capillaries, cut off the blood-supply from the impacted areas, and thus mechanically and by their toxic secretions cause necrosis of circumscribed patches of the hepatic substance.

Pyæmia is thus found to follow wounds and injuries, especially resection, amputation, and gun-shot wounds; or it is consecutive to suppuration in connection with bone, as in comminuted fractures and otitis; or arises in connection with suppurative processes in the bladder, prostate, or urethra; or in the uterus after parturition. It is also occasionally met with in ulcerative endocarditis and aortitis. It has been observed to follow trifling operations such as phlebotomy, local inflammations such as carbuncle and whitlow, and general diseases such as typhus, typhoid, rheumatism, and small-pox.

Bacteriology.—There is no evidence of the existence of a specific microbe of metastatic liver abscess, nor, indeed, of any form of suppurative hepatitis. Rosenbach found the streptococcus pyogenes in five out of six cases of pyæmia; twice associated with staphylococcus pyogenes aureus, and in one case, which ended in recovery, the staphylococcus was discovered alone (3). In pyæmia associated with ulcerative endocarditis or osteomyelitis, staphylococci (aureus and albus) have been demonstrated.

Morbid anatomy.—The liver is studded with small abscesses containing thick pus of a white, yellow, or greenish colour. The abscesses may be disseminated, or arranged in clusters in different parts of the liver; but are often most numerous towards the surface of the organ. The abscesses are generally surrounded with a zone of congestion; their walls, in most cases, being formed by the hepatic substance and devoid of any limiting membrane. When the abscesses are few in number the intervening hepatic substance may be healthy. More frequently the liver is enlarged, softened, and friable; and it may be remarked that in pyæmia the liver is often enough found enlarged, softened, and of an oily appearance; it may even contain pyogenetic micrococci without being the seat of suppuration—death having anticipated this result. Coming to the formation of these abscesses, we find that the infective agents reach the capillaries of the liver through the hepatic artery, and ultimately invade the finer veins. The lumen of the affected vessels is obliterated, the supply of blood to the corresponding hepatic territory is cut off, and, as a *result, we have cloudy swelling of the hepatic cells, disappearance of their* nuclei, and breaking down of their protoplasm; the destruction of tissue being doubtless furthered by the chemical action of the products of the microbes.

While these changes are in progress small-celled infiltration makes its appearance in connection with the finer veins—interlobular and central. Pus forms and, mixing with the necrosed hepatic tissue, gives rise to an abscess.

In its nascent stage the abscess appears as a buff-coloured patch of normal consistence, but somewhat swollen, so that the parenchyma in which it is seated is slightly prominent. Each necrotic patch corresponds to a group of lobules related to one of the smaller divisions of the portal vein, on which they are placed like leaves on a twig. After a time these patches soften from the centre, forming spheroidal abscesses varying in size from a millet seed to that of a walnut: these, in number, correspond to the microbic emboli impacted in the liver, and in their stages of growth to the successive dates at which the impactions have occurred.

While the multiple abscess affecting various organs is eminently characteristic of the pyæmic process, it occasionally happens that the liver alone is the seat of suppuration after surgical operations; and in such instances it is not unusual to find one or more large abscesses present. A case of this kind is recorded by Vedrènes, in which repeated chills occurred on the twenty-first day after a sword-wound of the head. This was followed by pain in the region of the liver, the formation of a fluctuating tumour, the evacuation of half a tumblerful of pus, and eventual recovery. Trousseau, again, relates the case of a man who died, with all the symptoms of purulent infection, fifteen days after an operation for comminuted fracture of the humerus. At the autopsy enormous abscesses were found in the liver, apparently without any deposits in other organs, or any discoverable inflammation of the veins leading from the stump. Still more rare is it to meet with a solitary liver abscess when other internal organs are the seat of metastatic deposits. Guthrie relates a case which appears to have been of this nature: the patient was a soldier who had been wounded in the battle of Waterloo, in whom amputation of the right arm had been performed. He died after exhibiting pronounced febrile symptoms and a tendency to delirium. The pleura pulmonalis on both sides was covered with a thick layer of coagulated lymph; a quantity of serum occupied the left side of the chest, and the pericardium was distended with fluid. The liver, enormously enlarged, pushing up the diaphragm and displacing the lung, had in its substance a large abscess containing at least a quart of pus (7). But, in pyæmia the liver is seldom the only or even the most common seat of metastatic suppurations. According to Sedillot's figures, the lungs are affected in 99 per cent, the liver and spleen in 8·3 per cent, the muscles in 6·6 per cent, and the heart in 5 per cent of the cases of pyæmia.

Symptoms.—*When it follows surgical operations, pyæmia may appear at any time from within a few days of the operation until the wound is thoroughly healed.* After parturition it usually manifests itself between the third and fifteenth days. The wound assumes an unhealthy appearance, the discharge becomes scanty, fœtid, or otherwise changed in character; in puerperal women the lochia become offensive, scanty, or arrested. The disease declares itself by rigors—repeated, it may be, two or three times daily—followed by hyperpyrexia, rapid defervescence, and profuse sweating. These attacks are renewed at irregular intervals, while metastatic deposits take place in the lungs and other internal organs; or in the joints, muscles, or subcutaneous tissue.

These deposits are further announced by symptoms special to the organ affected. The deposition of pus in the liver is indicated by pain in the hepatic region—a symptom, however, which is sometimes absent or only elicited by pressure—and by a uniform enlargement of the organ, which, in most instances, may be detected by careful palpation and percussion if the patient survive the attack for a few days. The general aspect of the patient betrays the serious nature of the malady from which he is suffering. The countenance undergoes a change expressive not so much of pain as of oppression. Emaciation proceeds rapidly The heart's action is hurried and feeble; the respiration shallow and accelerated; the skin assumes an icteric or subicteric tint even in cases in which the liver is not the seat of abscess; the urine contains bile pigment; albumin in small amount may be present, and the urea is increased. Diarrhœa almost invariably supervenes, and vomiting is frequently present. The mind may remain clear until the end, or the patient sinks into a typhoid condition marked by drowsiness, muttering delirium, subsultus tendinum, and, ultimately, coma. Death generally occurs between the third and twelfth days.

Diagnosis.—The presence of a wound or injury, or the history of a recent confinement, gives pathognomonic significance to the rigors, fever, and sweating. The sudden, tumultuous, febrile outburst, the irregularity of the accessions, the violent constitutional and local symptoms, which so speedily follow, will make the pyæmic nature of the case sufficiently obvious; but at the same time they may divert attention from the liver complication. Pain, sharp or obtuse, uneasiness or a feeling of weight or tension in the region of the liver, pain or tenderness on pressure, and more or less enlargement of the organ should lead us to suspect that the liver is attacked. Icterus and enlargement alone, without pain, are of less diagnostic significance, inasmuch as they are frequently present in pyæmia when suppurative hepatitis is absent.

Prognosis.—Pyæmia with diffuse visceral metastatic deposits has almost invariably one termination—death. The recorded instances of recovery refer mostly to cases in which the localisations were wholly or mainly confined to external organs. Occasionally when the liver alone of internal organs has been the seat of abscess-formation, and the abscesses have been few, or have coalesced into one collection, recovery has taken place; but cases of this nature are extremely rare.

Treatment.—The treatment of pyæmic suppurative hepatitis is mainly that of pyæmia, for which the reader is referred to the article on the subject [vol. i. p. 586]. Should it happen that one or more large abscesses are formed, surgical interference becomes practicable.

PORTO-PYÆMIC LIVER ABSCESS—PYLEPHLEBITIS.—**Etiology.**—Portal pyæmia is characterised anatomically by having for its cause a lesion situated within the portal tract, and by the restriction of the metastatic process to the liver. These peculiarities involve important modifications in the clinical phenomena of the disease which we shall have afterwards to describe.

The frequency with which metastatic abscesses are met with in the liver in connection with unhealthy suppuration within the portal territory is less than might have been expected, considering the liability of the gastro-intestinal canal and its annexes to suppurative processes, and the constant presence of pyogenetic micro-organisms in the digestive canal. Nor, as might have been expected, is it the pyæmic form of suppurative hepatitis that is most frequently observed when abscess of the liver complicates tropical dysentery. The doctrine of Budd - that abscess of the liver, arising during the progress of dysentery, is always of pyæmic origin—is opposed to the fact that the autopsies in such cases reveal more frequently one large abscess than two, and two large abscesses more frequently than the multiple, small, disseminated deposits characteristic of pyæmia. In two instances in which I have had an opportunity of examining the liver at quite an early stage of abscess-formation, secondary to dysentery, I found the solitary, large, necrotic focus present in both. Similar observations have been recorded by Kelsch and Kiener (9) and by Morehead. But if, in the face of such facts, we cannot concede that important part to portal pyæmia in connection with suppurative hepatitis secondary to dysentery which some have claimed for it, we must not, on the other hand, overlook the tendency of disseminated abscesses, distributed as they sometimes are in groups, to coalesce so as to form large abscesses. It cannot be doubted that in a considerable number of instances the larger multiple abscesses associated with dysentery are of pyæmic origin. The proof of this is sometimes found in the traces of the outlines of smaller cavities on the walls of a large abscess. But allowing, for this process of coalescence, it may, we think, be safely affirmed that, the pyæmic liver abscess does not form more than ten per cent of the cases of suppurative hepatitis associated with dysentery.

The existence of phlebitis and the presence of pus and decomposing clots in the veins have been demonstrated in a certain number of cases of dysentery. In seventeen cases the autopsy revealed sloughing or gangrenous ulceration of the large intestine, and in a great majority of these the cæcum was the part chiefly affected. In two of the cases large portions of the mucous membrane of the bowel had been passed by stool. In others, the large intestine was ulcerated throughout and often thickened. In one case only did the ulcerative process in the large intestine appear to have been of a minor grade. We may conclude, therefore, that unhealthy suppuration in any portion of the portal tract may give rise to pyæmic abscess in the liver; and that sloughing of the submucous connective tissue of the bowel, in which the radicles of the portal vein are necessarily involved, is the form of lesion most frequently observed when the pyæmic process is consequent on dysentery.

Pathology.—The pathology of portal pyæmia differs in no respect from that of general pyæmia. In the former, as in the latter, we have to do with a process of capillary embolism resulting from the impaction of masses of pyogenetic micro-organisms, or of infected particles leading to necrosis of the hepatic cells and proliferation of the connective tissue elements with suppuration.

Morbid anatomy.—When the vena porta contains decomposing clots, the abscesses are invariably numerous or innumerable, and devoid of any limiting membrane. In a case recorded by Marston, arising from a semi-gangrenous condition of the appendix vermiformis and cæcum, the liver was enlarged, full of small abscesses from the size of a millet seed to that of a walnut, "spreading out from the branches of the portal veins like twigs from a tree." They were destitute of a limiting membrane, and the lobules were surrounded by dark rings of congestion at the parts least affected. The pus in these cases is thick, and white, sometimes with a tinge of yellow or green, rarely red-coloured and sanious.

When the disease arises from limited points of ulceration in the gastro-intestinal canal, in the bile-ducts, or gall-bladder, without the presence of clot or pus in the larger vessels, the abscesses vary much in number. In some instances seven or eight only have been found; in other cases from forty to fifty; frequently they are to be reckoned by hundreds. They are generally found in both lobes, although seldom to the same extent, and they are often most numerous towards the surface. Occasionally they are distributed in clusters in limited portions of the hepatic substance. Along with these purulent foci we frequently meet with sharply-defined pale yellow patches, from three to twenty lines in diameter, some of which are consistent throughout—perhaps even more firm than the healthy liver substance—while others are softened in the centre. Some of them are surrounded with rings of congestion, others are without a trace of hyperæmia. When the abscesses are few in number, the intervening liver substance is microscopically healthy; but if the deposits are numerous, the liver is more or less congested. Whether few or many, the organ, as a rule, is enlarged. When the deposits are limited to one lobe, it is enlarged and more or less congested; while the other lobe may be healthy or only slightly congested. How completely confined to one lobe the disease may sometimes be, will be seen by referring to the beautiful plate given by Annesley (*Diseases of India*), illustrating case lxxvii., in which the left lobe appears of normal size and perfectly healthy; the lobules being distinct and well marked, while the right lobe is much enlarged and of a deep purple colour.

When the disease supervenes on chronic dysentery, the liver throughout, or in certain areas, is more or less diseased—often softened and easily broken up, or firm but friable, and of a pale drab or yellow colour. When the pyæmic suppuration appears during the course of acute dysentery the hepatic substance often presents a healthy appearance; but there are many exceptions to these rules.

When the patient has survived the attack for some time the abscesses become encysted. Louis, in one of his cases, found the cavities lined by a membrane half a millimetre thick, which was soft yet susceptible of removal by traction (11). In a case associated with dysentery, recorded by Morehead, the history of which did not extend beyond sixteen days, "the liver was studded with abscesses about the size of walnuts, each within a membranous bag" (17).

The spleen is generally healthy. In some instances it has been found smaller than normal and firm; or, on the other hand, much enlarged and softened. But the morbid appearances found in this organ are not, as a rule, causally related to the hepatic disease.

Although it is distinctive of portal pyæmia that the liver acts as a barrier to the passage of the infective micro-organisms into the general circulation, so that metastatic abscesses of other organs are seldom met with in this form of pyæmia, nevertheless instances do occur in which the disease becomes generalised. Dance records an interesting case of this kind in which ulceration and disorganisation of the common bile-duct extended to the portal veins, penetrating their cavities by small openings, and thus allowing the bile (probably along with other matters) to enter into the circulation. The portal veins contained clots and pus. In addition to numerous abscesses of the liver there were petechiæ, pustules, and gangrene of the skin, with numerous metastatic abscesses in the lungs, muscles, and parotid gland (5).

Symptoms.—The symptoms of liver abscess due to portal pyæmia vary according to the presence or absence of phlebitis, the organ which is the seat of the primary lesion, and the extent to which the liver itself is involved. I shall, therefore, briefly particularise the symptoms met with in certain groups of cases, illustrating special features from my own experience and that of others.

It is exceptional for the advent of portal pyæmia to declare itself by an array of symptoms so obtrusive and distinctive as those that usher in the general pyæmic infection. It is mostly when the disease is associated with decomposing clots or pus in the portal vein, or some of its larger branches, that severe rigors and sweating are observed. In a case observed by Busk (2), in which a suppurating mesenteric gland had burst into the trunk of the portal vein, there were frequent rigors followed by lobe the disease may sometimes be, will be seen by referring to the beautiful plate given by Annesley (*Diseases of India*), illustrating case lxxvii., in which the left lobe appears of normal size and perfectly healthy; the lobules being distinct and well marked, while the right lobe is much enlarged and of a deep purple colour.

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When portal pyæmia is dependent on ulceration of the stomach there will usually be a history of gastric troubles pointing towards ulceration. The liver complication generally begins with the milder train of symptoms just enumerated, and are often somewhat ambiguous in their nature. In a case recorded by Louis the liver disease set in with jaundice, headache, pains in the limbs and loins, anorexia, great thirst, and a dull pain in the epigastrium. There was a feeling of resistance or fulness in the right hypochondrium, the pulse was rapid, and the skin hot and dry. Then followed severe pain in the region of the gall-bladder, and during the last eight days of illness there were diarrhœa, nausea and prostration. There were no rigors throughout the whole course of the disease. On examination the liver was found enlarged, softened and ecchymosed at points, and contained a great number of encysted abscesses from four to five lines in diameter. In a case which came under my own observation the symptoms were much more distinctive. Symptoms of chronic ulceration of the stomach were followed by irregular chills, fever, and moisture of the skin, with marked pain in the hepatic region—especially in the right hypochondrium—slight enlargement of the organ, vomiting, diarrhœa, and great prostration. There were about thirty small, non-encysted abscesses scattered through the right lobe, from the size of a hazel-nut to that of a walnut, and a few smaller points of suppuration in the left lobe.

When ulceration of the gall-bladder or obstruction of the bile-ducts is the primary lesion, the symptoms—other than those of a typhoid type—are by no means uniform. We may expect in these cases a history of biliary colic. Gall-stones or suppuration in the gall-bladder may lead to multiple abscess in the liver in two ways—(i.) by extension to the portal vein, the bile-ducts being healthy; (ii.) by setting up suppurative cholangitis (*vide* art. "Cholangitis," p. 249). Suppuration is frequently announced by irregular febrile accessions and sweating. Sometimes fever alone, without rigors or sweating, is present. Pain is generally complained of, but is often referred at the beginning to the epigastrium, less frequently and distinctly to the right or left hypochondrium; although at a later stage of the disease pressure over the hepatic region seldom fails to elicit signs of pain. Enlargement of the organ will be made out by palpation and percussion. Vomiting and jaundice are often present in this form, but have little pathognomonic significance. Upon the whole, fever, pain in the hepatic region, and enlargement are the symptoms which point most directly to suppuration. The pyæmic nature *of the disease must be inferred from the accompanying constitutional symptoms, which we have spoken of as "typhoid." The patient's* features become suddenly shrunken; prostration, oppression, cold sweats, and diarrhœa set in. The mind may remain clear until the last, but in many cases stupor and delirium set in before death. One or more of the initial symptoms may be absent; the typhoid condition never fails to make its appearance.

Febrile symptoms may usher in pyæmia when it follows operations on the rectum, or disease of this part; but in some instances the sudden supervention of typhoid symptoms has been the first indication of the disease. There may be little complaint of pain in the region of the liver in such cases, and the invasion may consequently be overlooked unless sought for; but a careful examination of the organ will usually reveal the presence both of pain and enlargement. After repeated and violent attempts to reduce a prolapsed anus, Cruveilhier observed the expression of the patient to change on the same day (an important indication of pyæmic mischief). The pulse became small and frequent; the patient fell into a state of prostration, with cold skin, vomiting, hiccup, and stupor, but without much pain, and died on the fifth day after the operation.

When pyæmic abscesses in the liver occur during the course of dysentery, the symptoms of hepatic suppuration will, in most cases, be recognised, unless indeed the attention be absorbed by the urgency of the primary disease. The supervention of fever, during the progress of dysentery, or its marked increase should suffice to direct attention to the liver. If suppuration is detected, its pyæmic character will be inferred from the uniform enlargement of the organ, the absence of bulging or localised pain, and, above all, from the rapid development of the train of symptoms which we have already described. Should the dysenteric symptoms point to sloughing of the large intestine, this will naturally give increased significance to the other phenomena indicative of pyæmia.

Diagnosis.—If we compare the symptoms of portal with those of general pyæmia, two features become apparent at once. Those symptoms of the general infection which depend on localisations in the lungs, spleen, kidneys, heart, joints, and connective tissue are absent in portal pyæmia. In most instances also, as we have seen, rigors and sweats are less frequent, less severe, and persistent, or even altogether wanting. The other symptoms significant of a general pyosepticæmic infection of the system are present, and pretty much alike in both forms. The patient's features become pinched, anxious, and pale; he is dull and drowsy or restless and agitated, there is a feeling and appearance of great oppression, the skin and conjunctivæ become sallow or jaundiced, there are cold sweats, thirst, hurried, feeble and irregular action of the heart, rapid emaciation and diarrhœa ending in exhaustion or coma. These symptoms appearing during the progress of a disease associated with ulceration or sloughing within the portal tract, accompanied by the usual signs of hepatic suppuration, *indicate the formation of pyæmic abscesses in the liver.*

Kelsch and Kiener, who have not recognised the distinction between portal and general pyæmia on the one hand, or between the pyæmic and tropical form of liver abscess associated with dysentery on the other, have nevertheless drawn attention in a very particular manner to the frequency with which the train of symptoms I have just enumerated are found related to multiple and small abscesses of the liver. "Our inquiry," they say, "has shown us the frequent correlation between acute hepatitis accompanied with more or less marked typhoid symptoms and the multiplicity and smallness of the purulent foci. This correlation is affirmed by facts sufficiently numerous to warrant our bringing it into relief" (10). The facts lead us farther, and justify the distinction here made between portal and general pyæmia, and between portal pyæmia and the liver abscess usually associated with tropical dysentery. Typhoid symptoms, similar to those met with in pyæmia, appear in connection with the formation of the multiple pyosepticæmic deposits following the opening of a tropical abscess; and also as a result of purulent absorption from an unopened abscess. In neither case can the symptoms be mistaken for those of portal pyæmia.

Prognosis.—It is unnecessary to say that the prognosis is always highly unfavourable. Recovery, no doubt, occasionally takes place by absorption when the abscesses are few, or by the fusion of a group of smaller purulent foci into a single abscess and its subsequent spontaneous or operative evacuation.

Treatment.—Our chief hope in this disease clearly lies in prophylaxis. The mildest forms of inflammatory action in any part of the portal tract should be looked upon as serious from their possible results; and the appropriate remedies should be sedulously employed. Asepsis of the intestinal canal should also be maintained so far as possible by the means indicated in the article on Dysentery (vol. ii. p. 435). When, notwithstanding these precautions, the disease has arisen, the medical treatment will be that of pyæmia, and the surgical treatment that of liver abscess.

SECONDARY PYOSEPTICÆMIC ABSCESS OF THE LIVER.—This form of hepatic suppuration is always secondary to the opening—spontaneous or operative—of an abscess of the liver, and the consequent entrance of infective micro-organisms from without. It is thus met with as a sequel of the bursting of an abscess into the lung or bowel; but much more frequently it follows the opening of an abscess externally. Notwithstanding the use of antiseptics, secondary pyosepticæmia is still the danger which the surgeon has most to dread in operating for liver abscess.

The anatomical character of pyosepticæmia is the appearance in the immediate vicinity of the primary abscess—occasionally, also, in other parts of the organ—of small abscesses from the size of a pea to that of a walnut, or even larger. They are often surrounded by a ring of congestion, and are destitute of pyogenetic membrane. Their contents may be either a white pus or a reddish serous fluid. Sometimes small, buff-coloured circumscribed nodules are also met with in various stages of abscess-formation.

Symptoms.—The external wound often assumes a sloughy gangrenous appearance. The discharge from the abscess may become scanty, serous, and of a red colour; in some cases it remains free from odour, in others it becomes fœtid. The walls of the abscess cavity are sloughy or necrosed.

The constitutional symptoms are similar to those of pyæmic abscess—pinched features, febrile accessions, sweating, diarrhœa, rapid loss of strength and collapse.

REFERENCES

1. Bryant. *Atlas of Pathology*, Syd. Soc. plate xxiv.—2. Budd. *Diseases of the Liver*, Lond. 1815, p. 139.—3. Cheyne. *Microparasites in Disease*, Syd. Soc. 1886. p. 432.—4. Cruveilhier, quoted by Budd, *op. cit* p 56—5. Dance *Archives gén de méd.* vol. xix. p. 40—6. Davidson. *Hygiene and Diseases of Warm Climates*, Edin. 1893, p. 631. 7. Guthrie's *Commentaries*, 5th ed. p. 63.—8. Hewett *Year-Book*, Syd. Soc. 1862, p. 210.—9. Kelsch and Kiener. *Traité des malad. des pays chauds*, Paris, 1889, p 187.—10 *Ibid.* p. 249—11. Louis. *Mém. ou Recherches anatom.-path.* Paris, 1826, Obs iv.—12. Marston, in Cooper's *Surgical Dict.* vol. ii p. 503.—13. Morehead's *Clin Researches*, 2nd ed. p 331, case 97.—14. Sedillot *De l'infect. purulente ou Pyohémie.* Paris, 1849. 15 Trousseau. *Clin. Med.* vol v. p. 262.—16. Vedrènes. *Rec de mém. de méd. mil.* 1869—17. Waring's *Enquiry into the Path. of Liver Abscess*, Trevandrum, 1854, p. 36.—18. Wilks' Report on Pyæmia, *Guy's Hosp. Reports*, Series III. vol. vii. 1861.

Tropical suppurative hepatitis.—**Definition.**—*Clinically*, tropical hepatitis presents itself as a febrile hyperæmia associated with dysentery, or independent of it, and terminating in resolution or suppuration. In cases which do not end in resolution, it is *anatomically* characterised by the formation of one or more large foci of microbic necrosis, at first diffuse, afterwards limited by a pyogenetic membrane. *Etiologically*, it is the expression of hepatic insufficiency, the result of the imperfect adaptation of the liver and associated organs to the physiological conditions—climatic and other—imposed upon them, leading to functional and nutritive changes which determine the invasion of limited areas of the hepatic parenchyma by pyogenetic bacteria.

Etiology.—*Geographical distribution.*—One of the most striking features in the etiology of this form of suppurative hepatitis is its practical restriction to tropical and subtropical regions. The large liver abscess, except as the result of injury, counts, as Hirsch remarks, among the rarest of diseases in temperate and cold climates. It is only in the extreme south of Europe that it becomes endemic in a mild degree. The relative frequency of liver abscess in certain geographical regions is approximately *measured by the death-rates from hepatitis among the troops stationed in them.* The figures in the following table refer to the four years 1888-91, except for Bengal, China, the Straits Settlements, and Egypt. For the first the average is for the three years 1888-90; for the second and third, 1889-91; and for the fourth, 1888 and 1889 only.

DEATH-RATES from Hepatitis per 1000 of the troops stationed in India and other British Possessions.

Country.	Death-rate.	Country.	Death-rate.	Country.	Death-rate.
Bengal	1·35	China . .	0·24	West Indies .	0·23
Madras .	1·78	Mauritius	1·48	Bermuda .	0·00
Bombay	0·96	South Africa	0·23	Canada .	0·00
Ceylon	0·88	Egypt	1·18	Gibraltar .	0·11
Straits Settlements	0·00	Malta .	0·43		

The fact that no death from liver abscess occurred in the Straits Settlements during the years included in this table sufficiently proves, what is otherwise well attested, that under ordinary circumstances these Settlements enjoy as marked an immunity from hepatic abscess as they do from malaria and dysentery. The experience of campaigns in the Malayan Peninsula has shown, however, that these diseases are rather latent in the nosology of the Straits than absent from it. Hepatitis, dysentery, and remittent fever were found by Conwell to be the reigning maladies among the European troops in the Island of Penang in the early days of its occupation. No satisfactory explanation has been given of the greater fatality of liver abscess in India, Ceylon, and Mauritius, as compared with the West Indies, where the climate is eminently tropical. It has been thought that the insular and more equable climate of the West Indies, and the mitigating influence of the sea-breezes on the temperature, go far to account for the lesser prevalence of suppurative hepatitis in these islands. Among the negro population, too, of the West Indies the disease must be exceedingly rare; for Dr. Macnaught did not meet with a single case of liver abscess in a negro during a residence of twenty-two years in Jamaica.

A brief notice of the distribution of liver abscess in other tropical countries must suffice as supplementary to the table given above.

In Africa, abscess of the liver is endemic in a mild degree both in Algeria and Tunis. The mortality from this cause in the hospitals of Philippeville and Bougie (1867-78) formed from 12·4 to 9·6 per 1000 of the deaths from all causes. The British troops in Egypt, as we have seen, suffer to a considerable extent, but Dr. Sandwith, whose long residence in the country lends weight to his observations, informs me that abscess of the liver is only met with among those of the natives who are addicted to the use of alcohol; while the orthodox Mussulman, who restricts himself to water, although he may suffer from hepatic enlargement is seldom the subject of suppurative hepatitis.

In Senegal, abscess of the liver is one of the most fatal diseases of the European residents, causing one-third or more of the total mortality; but here, too, it seldom affects the natives. In the French Soudan and the Upper Congo it is rarely met with except in connection with dysentery and diarrhœa. Along the east coast and inland regions of Africa, where dysentery is common and fatal, abscess of the liver is said to be comparatively rare. As regards the island of Zanzibar, in particular, we have the recent and explicit testimony of Drago to the effect that hepatitis and abscess of the liver are almost unknown there. Dysentery and liver abscess are alike prevalent in Mauritius, and the latter is by no means restricted to the white population. Here in a large proportion of cases these two diseases run their course independently of each other. In the Seychelles group, again, malaria is unknown, dysentery exceedingly fatal, and abscess of the liver only moderately prevalent.

Turning to Asia, it may be noted that suppurative hepatitis is not severely endemic in Cochin China, where it furnished (1861-64) a proportion of one in fifty-four deaths. In Tonkin it gives rise to about 3 per cent of the total mortality among the French troops.

Our accounts of the extent to which liver abscess prevails in the lowlands of Mexico and Central America are far from precise, but they justify the conclusion that it forms a much less important element in the pathology of the Western than of the Eastern Hemisphere. In British Guiana suppurative hepatitis is not, upon the whole, of frequent occurrence. Out of 457 consecutive autopsies made in the Georgetown hospital, we find no more than two cases of liver abscess mentioned; and the disease furnished only 21 admissions during the four years 1886-89, out of nearly 30,000 patients. Nor does it appear to be more common in the neighbouring countries of Surinam and Cayenne. The statements respecting Brazil seem to point to its somewhat frequent occurrence in certain districts, but it does not appear to be severely endemic in any part of the country.

In contrast to the comparative immunity from liver abscess which these regions enjoy, is its marked fatality along the shores of Peru and Chili. About 21 per cent of the subjects sent to the anatomical theatre in Valparaiso were found to have liver abscess. This points to its extreme frequency at any rate among the poorer classes in that city. In the more temperate districts of Chili south of latitude 35°, abscess of the liver ceases to be endemic.

A review of the geographical relations of hepatic abscess appears to warrant the following conclusions: (*a*) Abscess of the liver is practically restricted to, and is everywhere more or less prevalent in tropical and subtropical regions. (*b*) Its frequency in warm climates does not bear a strict relation to latitude or mean temperature. Those tropical countries, such as the Straits Settlements and Guiana, in which liver abscess is comparatively rare, are distinguished by an equable and moist climate; while many of the regions in which suppurative hepatitis is severely endemic are characterised either by great ranges or sudden transitions of temperature. In Senegal, for example, where liver abscess is so fatal, the temperature during the day may reach from 95° to 104° F., falling at night to 64° or 60°. (*c*) Liver abscess exists in countries where malaria is unknown, as in the Seychelles group, the island of Rodrigues, and also in Chili and Mauritius, in both of which malaria has only appeared in quite recent times. On the other hand, it is never absent from the pathology of a tropical country in which dysentery is endemic; although the facts, so far as they are ascertained, do not support the sweeping conclusion of Chauffart that "the more frequent, grave, and persistent dysentery is in a country, in the like proportion will suppurative hepatitis be frequent, persistent, and grave." (*d*) In tropical countries ordinarily exempt from the malady it will appear in a severe form among Europeans subjected to unusual exposure and fatigue. (*e*) Dysentery and hepatic abscess may be prevalent in a given region, but, nevertheless, be to a large extent independent of each other.

Relation to altitude.—The occasional occurrence of hepatic abscess in Europeans transferred from a coast to a hill station is no more inconsistent with the fact that the disease becomes less frequent (other things being equal) in proportion as the increase in altitude reduces the temperature to that of higher latitudes, than its occasional occurrence in those who have returned to England is inconsistent with the proved immunity of temperate climates from liver abscess. Rouis states that in Algeria abscess of the liver is unknown or rare in localities such as Médéah, Milianah, etc., the altitude of which reaches or exceeds 1000 metres. Jourdanet likewise found the disease to be rare at the higher elevations in Mexico. A moderately elevated spot may, however, from local circumstances, be more productive of hepatitis than the sea-coast. Liver abscess is undoubtedly less fatal in the more elevated and colder districts of the North-West Provinces of India than in Lower Bengal. The death-rate from hepatitis in the Presidency district of Bengal (1881-88) was 1·85; in Peshawar, at an elevation of 1110 feet, it was 0·80 per 1000.

Meteorological conditions.—High temperature.—A careful consideration of the latitudinal and altitudinal relations of hepatic abscess points very conclusively to the influence of a high mean temperature as an important factor in its etiology. That the high temperature of the tropics, more than any concurrent meteorological element, is the chief climatic factor in determining the geographical distribution of liver abscess, is confirmed by the observation of Rouis that in Algeria those years when the heat was unusually severe, such as 1843, 1847, 1853, and 1849, never failed to furnish an increased number of cases of liver abscess, and that the disease is, upon the whole, most prevalent in localities where the temperature is excessively high. Budd ascribes the prevalence of abscess of the liver in the tropics to the greater frequency of dysentery in warm climates. But if heat plays no important part in the causation of tropical abscess, it is difficult to explain why it should become to such a large extent divorced from the dysentery of temperate climates. The objection urged by this distinguished authority against the influence of heat as a factor in the genesis of liver abscess, namely, that men employed in japanning, and other processes in the arts, are exposed to heat much greater than that of India, but do not suffer in consequence from liver abscess, is based, I venture to think, upon a defective appreciation of the conditions of life in the tropics. Nor is it to be admitted that those subjected to constant and great heat in temperate climates in connection with manufacturing processes never suffer from liver abscess. A typical case of the disease is recorded by Graves as having occurred in a robust man, by trade a glass-blower—an employment in which the workmen are subjected to intense heat. A closer examination into the history of the comparatively rare cases of idiopathic abscess met with in temperate climates must be made before Budd's statement, that those who are exposed to great heat in temperate climates do not suffer from liver abscess, can be accepted. In short, as Maclean has remarked, "it is impossible to overlook the influence of a continued high temperature in causing suppurative inflammation of the liver, although some esteemed authors have made light of it." I am inclined to place exposure to a constant high temperature in the first rank as a predisposing cause of tropical liver abscess; and clinical observations seem to show that, in exceptional instances, temporary exposure to excessive heat may also act as an exciting cause of the disease (9).

Vicissitudes of temperature.—In our review of the geographical distribution of liver abscess we have already observed its prevalence in regions where there are great, frequent, and sudden transitions of temperature. Clinical facts point clearly in many instances to a chill as the exciting cause of the disease in those whose constitution has been impaired by tropical heat. I may mention one case which came under my own observation in which the facts could bear one interpretation only. A young man belonging to the Indian population of Mauritius, who had previously enjoyed good health, and had never suffered from diarrhœa or dysentery, presented himself with an abscess in the right lobe of the liver. His account was that, being employed as a night guardian, he had spent the afternoon and evening drinking arrack with his companions. He fell asleep at night on the damp ground, and awoke next morning with severe pain in the right side, which persisted, and was soon followed by fever, and terminated in abscess. Instances of this nature are within the experience of all who have had occasion to see much of the disease.

Sir Ranald Martin states that he frequently observed acute inflammation of the liver follow exposure to a cold north wind in people issuing from heated ball-rooms in Calcutta (Maclean). Larrey, in his account of the French campaigns in Egypt and Syria, gives it as the result of his experience that suppression of the perspiration by a chill was one of the most frequent causes of liver abscess among the troops.

Personal influences.—*Age.*—Hepatic abscess is chiefly a disease of adult life. Among 23,850 soldiers' children in India, three deaths were caused by liver abscess—a ratio of 0·13 per 1000; which is about a tenth of the mortality of the army.

Sex.—Of 11,413 soldiers' wives, for which data are available, 8 died of abscess of the liver, or 0·70 per 1000, which is about one-half of the death-rate of the men. It may be assumed that among women of the higher classes liver abscess is still less common. The rarity with which women are attacked in Egypt has been noticed by several authors (7), and is confirmed by the testimony of Sandwith.

Race.—It is everywhere remarked that the natives of tropical countries are much less liable to suppurative hepatitis than Europeans. The death-rate per 1000 of the European troops from abscess of the liver in 1890 was 1·05, while that of the native army was 0·03—the death ratio of Europeans being thus thirty-five times higher than that of the natives of India. For the two preceding years the European death-rate was twenty-five times higher than that of the natives. We shall be the less disposed to exaggerate the admitted importance of dysentery as a factor in the causation of liver abscess if we bear in mind that dysentery is quite a common and fatal disease among the native races of India. No doubt the habits of the two races count for much in this connection.

Conwell states that "the native domestics who acquire European vices are equally or more subject to hepatitis than the Europeans." It may at least be said that their immunity from the disease is much lessened, by contracting drinking habits. I may remark that liver abscess is by no means rare among the coloured Creole and Indian populations of Mauritius. Respecting the comparative liability of Europeans of different nationalities to contract liver abscess on being removed to the tropics, we have the valuable but narrow experience of Haspel, who had charge of a foreign legion in Algeria. He found the Italians, Spaniards, and natives of the south of France to resist the diseases of Algeria (including hepatitis) infinitely better than the natives of the north of Europe. They proved, he says, physiologically better adapted to the country.

Acclimatisation.—Length of residence in the tropics does not diminish but rather tends to increase the liability of Europeans to suppurative inflammation of the liver; as will be seen from the following figures, by Brydon, relating to the European army of India (1873-76), and showing the proportion of deaths from liver abscess to 100 deaths from all causes at different periods of service:—

First four years	Fifth to seventh year	Above seven years
14·0	18 9	16·0

Food and Drink.—Free living, and an excessive use of animal food, when combined with want of exercise, have been looked upon as a cause of the disease. This may be true, perhaps, in respect to Europeans, but experience proves that it is seldom the penalty attached to errors of this kind in the case of natives who abstain from alcohol. The abuse of alcohol in any of its forms is one of the most potent of the remote causes of liver abscess. "We seldom," says Cayley, "meet with cases of hepatitis or liver abscess among total abstainers, except the pyæmic form directly associated with dysentery, but moderate drinkers are liable to suffer." I would only add that alcohol is also to be reckoned among the causes of liver abscess associated with dysentery.

Seasonal prevalence.—Hepatitis is everywhere most frequent after the heats of summer have exerted their depressing influence on the body, and the colder weather, with greater thermometrical fluctuations, sets in.

Relation to dysentery.—No point in connection with the ætiology of liver abscess has given rise to so many conflicting statements and hypotheses as that of its relation to dysentery. I shall here confine my attention solely to matters of fact. The frequency of dysentery as a complication of liver abscess is a matter of contention. Waring found ulceration of the large intestine in 147 out of 204 autopsies of persons who died of liver abscess—a ratio of 72·16 per cent. This agrees almost precisely with an analysis I have made of 111 cases reported by English and French authors. Kelsch and Kiener, on the other hand, found that 260 out of 314 cases, or 86 per cent, were complicated with dysentery, and they add that this proportion would have been still greater if they had taken into account 22 cases in which, according to the symptoms, dysentery had very probably occurred (15). It is upon these figures that the existence of liver abscess, not associated with dysentery, is declared by the French school to be quite an exceptional occurrence; and upon them is based the proposition that both are due to one microbic cause. To this school, indeed, liver abscess is but an incident in the course of dysentery. The latest figures bearing upon this problem, derived from the reports of the Sanitary Commissioners with the Government of India for the year 1892-93, show that the deaths from liver abscess numbered 137; and that of these only 58, or 42 3 per cent, were found associated with dysentery. If we are prepared to accept these figures as even approximately correct, we shall have to admit that the so-called idiopathic form is of much more frequent occurrence in India than the estimates derived from reported cases had hitherto led us to suppose; and if we bear in mind that most of the cases successfully operated on belong to the class of those not associated with dysentery, it will be evident that the proportion of cases treated in which the disease is independent of dysentery must be higher than the ratio given above, which is based upon necropsies. The frequency of a dysenteric complication in fatal cases of liver abscess doubtless varies in different countries and circumstances, but the view that uncomplicated cases form a quite unimportant residuum of the whole cannot be maintained.

What is, then, the frequency of hepatic abscess as a complication of dysentery? According to a very complete table compiled by Hirsch of 2377 autopsies of tropical dysentery, hepatic abscess was present in the ratio of 19·2 per cent, which agrees closely with the estimates arrived at from a much smaller number of autopsies made in Algeria. It is usually the severer cases of dysentery that become complicated with hepatitis. In forty-five autopsies of dysentery recorded by Morehead, four only were complicated with liver abscess, and in each of these sloughing lesions were present in the bowel (cases 59, 65, 72, 81).

When we turn to temperate climates, it is rare to find dysentery complicated with liver abscess. Thierfelder informs us that in 231 autopsies of persons who had died of dysentery in Prague between February 1846 and September 1848 no instance of abscess of the liver was found. The same was true in the eighty cases of epidemic dysentery observed by Niemeyer in the military hospital at Nancy and examined after death. Dr. Marston states that of the great number of soldiers from the Crimea suffering from dysentery who came under his charge in the Malta hospital, only two were subjects of liver abscess. Baly, again, did not meet with a single case of abscess of the liver in the many hundreds who died of dysentery at Millbank. It appears, however, to have been somewhat more common as a complication of the famine dysentery of Ireland; but accurate statistics of this epidemic are wanting.

As regards the priority of the diseases when found associated in tropical countries, we may state that, out of fifty-six observations bearing upon the point before us, the liver abscess and dysentery arose simultaneously in seventeen instances; the hepatic symptoms appeared at some time during the course of dysentery in twenty cases, and in four of these the dysenteric symptoms ceased or diminished as the hepatic disease appeared. In seven cases there had been a history of a previous dysenteric attack dating from six to twelve months before the onset of symptoms of liver disease. In twelve cases the hepatic symptoms had preceded the advent of the dysentery.

It is obvious from the facts before us that liver abscess often occurs as an uncomplicated disease, and that when complicated with dysentery it not infrequently precedes it. Yet on the other hand, if we bear in mind that in a varying, but still large, proportion of cases suppurative hepatitis is associated with dysentery, that, to a considerable extent, the two diseases are endemic in the same localities, and rise and fall in frequency synchronously, and that the one is often preceded or followed by the other, we shall be compelled to admit that the doctrine of simple coincidence is inadmissible. The nature of the relation between the two will be considered in the sequel.

Morbid anatomy.—In about 75 per cent of the cases the abscess is solitary, in 11 per cent double; while in about 14 per cent the number of abscesses exceeds two. These facts have an important bearing both on the pathology and prognosis of the disease.

In considerably more than half of the cases some portion of the right lobe—frequently its convex, upper, or outer surface—is affected. In its initial stage the abscess is generally seated at a greater or less depth within the substance of the liver; but in a certain number of instances (according to my observations, 6 to 9 per cent) it is superficial from the beginning.

The pus is generally thick and white, or tinged yellow or green; more rarely it is dark red or chocolate-coloured, and of the ordinary consistence or serous. Reddish serous contents are rather frequently found in the superficial abscess.[1] The quantity varies in amount from a few drachms to many pints. When the abscess enters its surgical phase the contents vary in amount from four to thirty ounces, or more.

In its first stage the abscess is diffuse; that is, it is limited only by the hepatic substance, which may be dense or softened; in the latter case it is found projecting in shreddy masses into the pus. At a later period the pus becomes limited by a capsule, which varies extremely both in thickness and consistence, and often presents internally a flocculent appearance. This membrane is formed of a granulation tissue, more or less highly organised, which makes its appearance at the line of demarcation between the dead and living hepatic substance.

The abscess thus limited, if small, may cease to extend. The pus becomes absorbed and the cavity undergoes obliteration, its site being marked by a white puckered cicatrix; or the contents may be reduced to a pulpy or chalky mass surrounded by a thickened capsule.

Much more frequently a liver abscess follows the course of an abscess in any other tissue, enlarging and making its way towards the surface by the disintegration of the intervening liver substance, and by the formation of minute points of suppuration in its walls which subsequently open into its cavity. During this process the vessels and ducts become obliterated; so that hæmorrhage or extensive extravasation of bile into the abscess cavity seldom occurs.

The patient may die before the abscess opens spontaneously, or is evacuated by operation. When spontaneous opening occurs, it will easily be understood, from what we know of the usual seat of the abscess, that it will generally make its way into the right lung or pleura. Very rarely, indeed, does it open into the pericardium. Rupture into the peritoneal cavity is a more common termination, and would be still more so if inflammatory adhesions of the abdominal viscera did not frequently circumscribe the pus and prevent its effusion. The transverse colon, again, gives issue to the pus in a certain number of cases. Less frequently the abscess opens into the stomach or duodenum; and the instances are quite exceptional in which the pus evacuates itself through the bile-ducts, the hepatic veins, the vena cava, or the pelvis of the right kidney.

Before the evacuation of the pus the liver, in nine cases out of ten, is enlarged, and this enlargement is looked for as one of the surest signs of abscess-formation. Rouis found, however, that when the pus had been got rid of, the volume of the liver was normal in about 63 per cent of his observations.

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[1] I am unable to offer any explanation of the serous character of the contents of the abscess in certain cases. Bacteriological research may, perhaps, throw some light on the matter. The point is deserving of investigation. To say that it is accidental explains nothing.

According to Waring, the substance of the liver, apart from the abscess and the immediately surrounding tissue, is generally congested, softened, or otherwise altered in colour or consistence. In only a few instances was it found to be perfectly healthy. Out of twenty-five observations recorded by Rouis, in which the state of the hepatic substance outside the abscess zone is minutely described, it was found to be more or less diseased in nineteen, and apparently healthy in six cases. Kelsch and Kiener's observations lead them to the conclusion that the integrity of the rest of the hepatic parenchyma is the rule and not the exception. My own observations point to the extreme rarity of a healthy state of the liver when abscess has followed repeated or long-continued attacks of dysentery. In these circumstances the parenchyma is manifestly diseased —often of a pale colour and friable, the lobulation being indistinct. In uncomplicated cases the liver substance is not infrequently healthy, except in the immediate neighbourhood of the abscess. Nor are we to assume that in every instance in which the hepatic parenchyma is found diseased on autopsy, it was so from the beginning of the suppurative process. The circumscribed nature of the lesion, and the frequency with which the liver proves capable of performing its functions after spontaneous or operative evacuation of the pus, point rather to the conclusion that the suppurative process in tropical abscess is a localised one dependent on nutritive conditions affecting primarily a limited area of the hepatic substance; exposing it to be surprised, as it were, by a microbic invasion which it was, perhaps only temporarily, unable to resist.

The lesions met with in other organs are somewhat numerous, but do not call for detailed description. The proximity of the advancing abscess on neighbouring organs and tissues, or its pressure upon them while it is making its way in the directions already mentioned, gives rise to adhesive inflammation of the pleural, pericardial, or peritoneal membranes; more rarely, to serous effusion into their cavities. Inflammation and ulceration of the intervening tissues, the rupture of purulent collections into one of the closed sacs or hollow viscera, and limited or diffuse abscess of the right lung are among the more common of the morbid conditions resulting from the spontaneous opening of a liver abscess.

The spleen, as a rule, is healthy; sometimes it is abnormally small, at other times enlarged; in either case its parenchyma may be softened or firm. Various morbid conditions have been observed in the kidneys, but none of them, except those mechanically produced, has any etiological significance.

Two special forms of abscess require brief notice: the fibrous abscess of Kelsch and Kiener, and the areolar abscess of Chauffart. The first is, multiple—numbering from three to twelve—the abscesses varying in size from a hazel-nut to that of a pigeon's egg, of a gray or whitish colour, and containing a grumous, semi-solid purulent matter. These small abscesses are characterised by their encapsulation in the midst of a stratified fibrous tissue which is traversed by numerous vessels with embryonic walls. The wall of the abscess is firm and coriaceous. The second form, advancing towards the surface of the liver, presents on section a series of unequal areolæ, isolated or communicating with each other so as to form a sort of cavernous structure. Each areola is lined with a pyogenetic membrane, and contains a muco-purulent fluid. This form is believed by Chauffart to be connected with inflammation of the biliary canals.

Nature and evolution of the lesions.—Side by side with a formed abscess we occasionally meet with the circumscribed buff-coloured patches or nodules already described in the section on pyæmia. Such a nodule, when softened at the centre, may be taken to represent the initial stage of a hepatic abscess; it is, in fact, an abscess in miniature. It is important to observe that, although in some cases the nodule is bounded by a hyperæmic zone, it happens quite as often that no such zone of congestion is present. We have before us, then, a group of lobules in a state of necrosis, the capillaries blocked, the hepatic cells in a state of cloudy swelling, or of advanced fatty and granular degeneration, with small-celled infiltration of the finer veins. The formed abscess, dysenteric or idiopathic, is in its earliest stage no more than a magnified necrotic nodule. As generally met with, an abscess at an early stage of its formation varies in size from that of a plum to that of an orange. On section the central portion is of a grayish yellow colour, and more or less diffluent. This central part is surrounded by a buff-coloured zone, the periphery of which is bounded by an area of congestion, from a quarter of an inch to an inch in breadth. This hyperæmia, as was pointed out long ago by Dr. F. N. Macnamara, who was one of the first to give an accurate account of the pathology of hepatic abscess, is secondary—a result of reaction. The process is essentially necrotic, not inflammatory. A microscopic examination of the fluid contents of the central portion confirms this view, for they are found to consist of broken-down liver-tissue—fat globules mixed with only a few scattered pus corpuscles.

To what is this process due? It has not yet been demonstrated for the tropical, as it has been for the pyæmic form of abscess, that the capillaries of the necrosed portions are impacted with micrococci. Yet the anatomical identity of the lesions in both speaks strongly for an identity of cause. In the abscess itself pyogenetic cocci have been frequently demonstrated. Macfadyen satisfied himself at once of the absence of amœbæ and of the presence of staphylococcus aureus in a case of tropical liver abscess contracted in India. In four out of nine cases of non-dysenteric liver abscess Kartulis isolated the same micro-organism, and in one case he demonstrated the S. albus. The same observer out of thirteen cases of dysenteric liver abscess demonstrated the S. aureus twice, the S. albus once, and the Bacillus pyogenes fœtidus once. The two staphylococci have also been found by Bertrand in liver abscess. That a considerable number of results have been negative does not prove that these microbes had not been present at an earlier stage. Thus it is in the highest degree probable that, when liver abscess is not associated with amœbæ, the impaction of pyogenetic micrococci in the capillaries of the necrosed area is the sole cause of tropical liver abscess; whether associated with dysentery or independent of it.

There is not much difficulty in accounting for the entrance of these organisms into the liver when the large intestine is the seat of dysenteric ulceration. The cylindrical epithelium, which forms the first line of defence from their inroads, is removed, and the exposed and injured vessels seem to invite their entrance. The difficulty of explaining their presence in the liver will appear at first sight to be greater when dysentery is absent. Birch-Hirschfeld recognises the probability of idiopathic liver abscess being a cryptogenetic infection, and suggests that the pyogenetic bacteria may obtain an entrance into the portal vessels through small excoriations in the intestinal tract; and we know how frequently a catarrhal condition of the intestinal canal, which must be accompanied by loosening and desquamation of the epithelium, is present at the beginning of suppurative hepatitis' But the assumption of wounds, large or small, is not at all necessary. It is well known that staphylococci have a considerable power of penetrating healthy tissue, and a still greater power of finding their way to diseased tissues. The biliary canals are normally aseptic up to a point near the entrance of the common bile-duct into the duodenum. If, however, obstruction of the common bile-duct be established by any extrinsic or intrinsic cause, the gall-bladder and biliary canals are speedily invaded by micro-organisms, and, amongst others, by staphylococci which, according to Netter's investigations, may penetrate into the liver and blood-vessels, and produce abscess of the liver and other organs (Macfadyen). [*Vide* art. "Cholangitis."] The unhealthy condition of the bile-ducts caused by the obstruction determines the immigration of the micrococci, and the absence of a wound does not prevent their access to the diseased tissues. There can be little doubt that these organisms, always present in the bowel, do from time to time enter the portal radicles and find their way into the liver; but there, if in small number and the liver functionally and structurally sound, they will be promptly destroyed. All the more certainly will they make their way into the organ if its vitality is impaired, and the greater will be their chance of establishing themselves in a given area if the endothelium of the vessels in that locality has from any cause become diseased. The importance of a lesion in disposing the part to the reception of infective agents has been demonstrated by Orth and Wyssokowitsch, who, according to Flugge (10), were able to set up endocarditis in rabbits by "first causing trivial lesions of the cardiac valves, and then injecting cultivations of staphylococci. The infection did not succeed when the cultivation was injected without simultaneous injury to the valve."

We have to bear in mind then, on the one hand, that a diseased condition of the liver, apart from wounds opening the lumen of the portal radicles, may determine an immigration of pyogenetic cocci; and, on the other hand, that an impairment of the vital energy of the endothelial cells of the capillaries is essential to the lodgment and increase of these organisms. The prevalence of liver abscess in the tropics, its comparative absence from temperate regions, and the singular fact that tropical abscess is a disease of the liver only, and not of any other organ or tissue, will become intelligible as soon as we can show in what manner and to what extent the transference of the European to warm climates gives rise to functional, nutritive, and structural disease of this organ.

The organs of the European have become adapted to work under the conditions which obtain in temperate climates. This is shown by the difficulty of rearing European children in India, and the constitutional degeneracy which results when they are not removed at an early age to their native country. In addition to this hereditary want of adaptation between European man and tropical surroundings, we have, in the case of those who are transplanted from a temperate to a tropical climate after reaching manhood, acquired habit to reckon with. Both of these elements vary greatly in different individuals. Some are better able to accommodate themselves to the new conditions of life than others. Without entering upon the vexed question of the additional work thrown upon the liver as the result of alterations of the respiratory function in warm climates, we may point out one respect in which the physiological balance is notably upset. The skin, which in temperate climates is comparatively inactive, is mainly related, vicariously, to the respiratory system. Hence a chill results in a catarrh of the respiratory tract. In the tropics, on the other hand, the functional activity of the skin is enormously increased, and it is now brought into close compensatory relationship to the portal system. A chill under the new conditions induces a congestion of the liver or an intestinal catarrh. Pathologically, this switching off of the skin from its connection with the respiratory and placing it in relation with the portal system (taken with correlated changes, of course), manifests itself in a complete alteration of the *cadre* of disease on transference to a tropical climate. The number of admissions from diseases of the respiratory organs falls from 57 to 32, while that from diseases of the digestive system rises from 101 to 143 per 1000. More particularly hepatic affections, mostly congestive, give rise to six times, and diarrhœa and dysentery to nearly ten times the number of admissions in India that they do in England. Congestion of the liver gives rise mechanically to congestion of the intestinal tract, and this mechanically caused congestion of the bowel is further aggravated by the physiological consequences of liver congestion. The circulation through the capillaries of the liver is slowed, the secretion of bile is consequently lessened, and the contents of the intestine, partially deprived of their antifermentative fluid, undergo fermentation, which in turn induces catarrh of the intestine already mechanically congested. One of the functions of the liver, which is believed to be closely allied to its glycogenetic function, is the transformation of toxins. These are the direct or indirect products of the bacteria which inhabit the bowel in the proportion, according to Vignal, of twenty millions to a decigramme of intestinal matter. The amount of toxins thrown upon the oppressed liver is augmented in intestinal catarrh and their character altered This still further increases the strain upon the organ, and, a vicious circle being thus established, it matters not whether the liver or bowel be the starting-point of the mischief ; the one acts and reacts upon the other, the result being disordered nutrition and impaired function in both, which disorder or defect, in some cases, runs on to structural change. The nexus, therefore, as we conceive it, between the dysentery of the tropics and liver abscess is to be looked for in the physiological and pathological relations between the two, rather than in any unity of pathogenetic germ. In a small but still considerable number of Europeans residing in tropical countries hepatic insufficiency exists, and all the more surely is this established if alcohol be taken to excess. The toxins, acting upon the tissues of the disabled liver, diminish their vitality, especially in parts in which previous congestions, or other causes, have already established an area of less resistance. It has been shown, as Flugge remarks, that, "under the influence of ptomaine poisoning, the same bacteria which formerly quickly died in the endothelial cells, and never caused disease in the animals, are now able to multiply with extreme rapidity and cause the death of the animals previously immune." There can be no difficulty, then, in understanding in what way residence in a warm climate causes hepatic insufficiency and, in so doing, favours the settlement and growth of pyogenetic organisms in the liver, quite apart from any dysenteric complication ; and also in what way and to what extent dysentery comes in as a powerful accessory cause of liver abscess. An attack of dysentery in temperate climates increases, it is true, the strain upon the liver, but the organ is sufficient for its work ; in a certain proportion of cases of tropical dysentery, however, the organ is unfit for the additional work thrown upon it. Dysentery at once favours the establishment of a point of less resistance, and, by the intestinal lesions it causes, facilitates the entrance of pyogenetic bacteria into the vena portæ. The attacks of febrile congestion of the liver, on the other hand, which are so frequently premonitory of abscess, determine, in the manner already indicated, a catarrhal or dysenteric inflammation of the large intestine, which in its turn aggravates the liver disorder.

Just as in temperate climates a blow over the liver, by impairing the vitality of the organ, furnishes the opportunity for an invasion of micrococci, so the want of adaptation of the organs of the European to the new conditions imposed upon them by transference to a warm climate frequently results in functional and nutritive changes in the liver which prepare it for the reception of the pathogenetic agents.

In tropical hepatitis pathological change in the liver is primary and determines the microbic infection. In pyæmic abscess, on the other hand, the impaction of minute infective emboli, derived from a local focus of unhealthy suppuration, in certain capillary areas to which chance may happen to direct them, is the primary lesion; and thus the further changes the liver substance may undergo are determined.

Symptomatology.—*Acute Hepatitis.*—Abscess of the liver is generally described as one of the terminations of acute hepatitis. The constitutional symptoms of hepatitis are fever, a coated tongue, constipation, scanty and high-coloured urine, gastric disturbance, and, in some cases, slight jaundice. The local symptoms are pain, tenderness, or simply a feeling of weight or uneasiness in the hepatic region, usually increased on pressure. Pain in the right shoulder occurs in relatively few cases, but when present it is an important sign of hepatic mischief. A uniform enlargement of the liver is the only other local sign of importance. If these symptoms do not subside spontaneously, or as the result of treatment, suppuration is to be feared. This event is announced by rigors and sweating, and by a bulging, painful enlargement in some part of the hepatic region.

Hepatitis thus clinically portrayed is not a fatal disease; 86 per cent of the cases treated by Morehead ended in recovery.

It may be safely affirmed that the vast majority of cases returned as hepatitis are febrile congestions of the liver due to malaria, having little or no tendency to end in suppuration. Hence it was that a free use of the lancet and mercury seemed so frequently to succeed in preventing this misfortune.

It must be admitted, however, that a form of hepatitis of a graver type, etiologically related to liver abscess, does occur The patient suffers from an attack characterised by the constitutional and local symptoms described above, and often in a severe form. In a few days it passes off, recurs, and again subsides. After, it may be, many such fugitive attacks the same train of symptoms reappears, not to pass off as before, but now as premonitory of liver abscess. In many instances this non-malarious hepatitis occurs in connection with recurrent dysenteric or diarrhœal attacks, and these should always excite suspicion, or it may appear as a primary disease. In either case it may be regarded as a febrile congestion resulting from the absorption of some ptomaine from the bowel. It points, in short, to toxic vulnerability, and is not to be regarded with indifference. It always indicates a state of things that may be followed by grave consequences, although it does not necessarily imply that an invasion of the liver by pyogenetic micrococci—the first step to abscess-formation—has actually taken place. This form of hepatitis, the only one relevant to liver abscess, has hitherto been very imperfectly distinguished from other forms, and it is very important that its nature and symptoms should be recognised and understood.

Liver Abscess.—The most distinctive symptoms of liver abscess are fever, pain, and irregular enlargement of the organ, followed by a train of phenomena secondary to suppuration, and significant of purulent absorption—emaciation, hectic, cold sweats, diarrhœa or dysentery, and occasionally delirium. It sometimes happens that all the symptoms, primary and secondary, are absent. In making autopsies one comes now and again quite unexpectedly upon an abscess which had not betrayed its presence by any symptom during life.

The evolution of liver abscess is so irregular that it is impossible to delineate the clinical features of the disease in such a way as to represent more than a few of its protean forms. I shall content myself, therefore, with a brief review of the individual symptoms, indicating, at the same time, the way in which they are usually found associated.

Fever.—In a very large number of cases fever is the initial symptom, and this may be accompanied from the beginning by pain in the region of the liver, and followed after a week or a fortnight by enlargement. In other cases the fever lasts for a period varying from a few days to a month or more before pain supervenes or distinctive enlargement can be made out. The fever sometimes assumes a quotidian type, or the accessions occur twice daily; but irregular evening exacerbations are most frequently observed, and these are usually followed by perspiration. The fever often subsides as the swelling appears, or even earlier; and may recur from time to time during the progress of the disease. The irregularity of the fever should excite suspicion of its non-malarial origin. Towards the end, fever of a hectic type is frequently present.

It is important to observe that in a few cases liver abscess makes its appearance suddenly with severe rigors, high fever, and urgent vomiting, and often enough without pain or tenderness in the hepatic region. An instance of this kind came under my observation which I mistook for and treated as a severe paroxysm of malarial fever. The diagnosis seemed to be justified by the disappearance of the symptoms within a few days. About eighteen months afterwards, during my absence, the patient was seized with all the symptoms of liver abscess and died. The autopsy revealed, in addition to a recent abscess, an old one, the size of a pigeon's egg, in the substance of the right lobe, advancing to cure. When we read of abscess being found in fatal cases of bilious remittent it means that a similar mistake in diagnosis has been made.

Pain.—In many cases pain is the first symptom to attract notice If its onset is sudden and severe it will be accompanied with more or less fever, otherwise it often persists for days or weeks without much fever or any enlargement. The pain is generally situated in the right or left hypochondrium or epigastrium; more rarely in the right shoulder, when it is generally found to be associated with abscess in the right lobe. If the disease be limited to the parenchyma the pain is usually dull and tensive, but when the serous capsule is involved it is acute and increased by superficial pressure.

Enlargement is one of the most common and distinctive characters of liver abscess. As a rule it follows the symptoms already mentioned. When the disease has made some progress it will frequently be possible to detect a bulging in some direction—upwards, downwards, or outwards—according to the seat of the disease and the direction it is taking. When it pushes up the diaphragm and encroaches on the thoracic cavity it often gives rise to a short, dry cough, dyspnœa, and oppression, with the physical signs of basal pleurisy or pneumonia; much more rarely does it cause hydrothorax. If the enlargement be downwards, the tumour will be felt below the margin of the ribs or in the epigastrium. By its pressure on the stomach, nausea, vomiting and other gastric symptoms may be caused. When the abscess comes into relation with the costal walls, more or less vaulting, with widening and effacement of the intercostal spaces, will be manifest.

Fluctuation can generally be made out when the abscess nears the surface.

Decubitus.—The patient is seldom able to lie on either side without suffering. In many cases he finds most ease by lying on his back with his shoulders raised.

Symptoms connected with the spontaneous opening of an abscess.—When the contents of an abscess are poured into the peritoneal cavity symptoms of acute peritonitis will speedily ensue. Pain in the region of the heart, a sense of suffocation, and the physical signs of pericardial effusion indicate rupture into the pericardium. Should the abscess burst into the right pleural sac, pain, dyspnœa, and the signs of pleuritic effusion will be present. If it burst into the lung, the sudden expectoration of brick-red puriform matter, sometimes tinged with bile, preceded and accompanied by the physical signs of pneumonia of the base, will be observed. Rupture of the abscess into the stomach is often preceded by gastric pain and irritation, and announces itself by purulent vomiting, or the pus, more or less changed, may pass off by the bowels. In case of rupture into the colon, pus will be detected in the stools, and a coincident subsidence of the tumour will be observed. The opening of the abscess into the pelvis of the right kidney can only be known by the discharge of pus by the urethra.

Duration, Diagnosis, Prognosis. — *Duration.* — Hepatic abscess running an acute course and ending fatally from seven to twenty-one days from the beginning of the disease is generally to be referred to portal pyæmia. Instances are occasionally observed, however, in which the tropical form proves fatal within a week or two. A case of this kind is recorded by Kelsch and Kiener as occurring in a patient who had been ailing for a few days only, and died six days after his admission to hospital. Tropical abscess, as a rule, runs a subacute or chronic course. The mean duration of fatal cases complicated with dysentery was found by Rouis to be ninety-five days, and that of those not so complicated eighty-five days. The cases ending in recovery ran a still more protracted course. The average stay in hospital of twenty fatal cases of which I have notes averaged forty-two days.

Diagnosis.—Hydatid cysts may be distinguished from liver abscess by their slow and painless growth; besides, they do not present the constitutional symptoms proper to liver abscess. A suppurating hydatid tumour will generally be recognised by the history of a previously existing painless and slowly increasing tumour; but in case of doubt an exploratory puncture should be resorted to.

An inflamed and distended gall-bladder has been mistaken for a liver abscess. The situation, the pear-like form, the mobility of the tumour, which, as Frerichs remarks, scarcely ever contracts adhesions to the abdominal wall, the absence of inflammatory œdema of the tissues over it, the history, in some instances, of biliary colic, and the fact that the tumour has been soft from the beginning, sufficiently indicate its nature.

Serious difficulty can scarcely arise in establishing a diagnosis between a deep abscess of the abdominal parietes and one of the liver. Should any doubtful case occur, the suggestion of Sachs to introduce a fine needle into the cavity of the abscess may be borne in mind; if the abscess be seated in the abdominal wall the needle will remain motionless during inspiration.

It is hardly necessary to do more than mention the possibility of a chronic liver abscess with hectic symptoms being mistaken for phthisis. The history of the case, the absence of the physical signs of tubercular deposit in the apex of the lung, the enlargement of the liver, and the local pain, are the points to be attended to.

The *prognosis* in liver abscess must always be guarded. Out of ninety-five admissions in the army of India in 1893, no fewer than sixty-two patients died. The coexistence of dysentery, the plurality of abscesses, a history of alcoholism, or the coexistence of severe constitutional disease all increase materially the gravity of the prognosis.

Treatment.—Our primary object must be the prevention of the disease. Much success in this direction has already been attained. The death-rate per 1000 in the European army of Bengal for the decennium 1860-69 was 3·31, and it had fallen to 1·00 in 1893. The effects of a constant high temperature can be largely mitigated by attention to the dwelling. The rooms should be large, airy, but not draughty. Needless exposure to heat should be avoided, and the clothing should be adapted to the climate. Care should also be taken to avoid exposure to chills, especially when heated, and to change the clothes as soon as possible when they have become damp with perspiration. Exercise, always short of exhaustion, should be taken regularly at proper hours. Excess of food and a diet below the requirements of the system are alike harmful. The habits and tastes of the individual are not to be ignored in advising the European respecting his regimen in the tropics. Some find themselves better on a diet chiefly animal, and have a difficulty in digesting food composed mainly of rice and vegetables. What is most easily digested will be found the best; but excess of animal food, rich sauces, and pastry should be strictly avoided. In some constitutions the lighter wines, taken in moderation and along with the meals, will not only be harmless but even beneficial. Ardent spirits in any form or amount are injurious, and ought to be shunned by every one who wishes to enjoy length of days and health in the tropics.

Attention to the regular action of the bowels will be looked upon as a matter of the first importance by those who share our views respecting the etiology of liver abscess. Constipation and looseness are alike to be guarded against. It should never be forgotten that, when either condition has become habitual, the patient is already in a state in which something more than a routine purgative or astringent is called for. There is something wrong in the food, drink, work, exercise, habits, or surroundings of the individual that must be looked into and set to rights.

A consideration of the important relations between dysentery and liver abscess will indicate the necessity of treating the mildest attack, especially mild recurrent attacks, of tropical dysentery as serious.

Care must be taken to distinguish the malarious from the non-malarious form of hepatitis. In the former there will usually be a history of previous attacks of ague; the spleen will probably be found enlarged, and the malarial parasite or pigment may be detected in the blood. The non-malarious form, as already stated, is frequently associated with recurrent diarrhœal or dysenteric symptoms. This form demands special treatment. The patient is to be confined to bed, his diet restricted to milk, and ipecacuanha given in full doses, whether diarrhœa or dysentery be present or not. Benzo-naphthol, or other appropriate antiseptic, should be administered in the intervals between the exhibition of the ipecacuanha. An occasional purgative dose of calomel or blue pill may sometimes be given with advantage, a practice often followed by a manifest improvement in the patient's feelings and the state of his excretions.

When the acute symptoms have passed or moderated, resort should be had to the chloride of ammonium in fifteen to twenty grain doses, three or four times daily, and persisted in for a considerable time, the action of the bowels must be regulated by cascara sagrada, a combination of euonymin and rhubarb, or an alkaline saline, as the special features of the case may suggest If pain or uneasiness in the region of the liver persist, successive applications of liquor epispasticus at various points over the seat of the pain will often give relief. But, above all, the habits of the patient as regards food, drink, and exercise should be regarded. If nothing in these respects seems amiss, and the hepatic symptoms persist, a change to a temperate climate must be made.

When abscess has formed, its treatment enters the domain of surgery. The earlier the existence of an abscess is ascertained, the greater will be the hope of successful surgical treatment. An exploratory puncture in case of doubt is all the more justifiable that the best results have been observed to follow its use, even when no abscess could be detected.

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REFERENCES

1. BIRCH-HIRSCHFELD. *Path. Anat.* Bd. xi. 2 Hälfte, Leip. 1895, p. 716.—2. *British Guiana Annual.* Georgetown, 1892.—3. BUDD. *Diseases of the Liver*, Lond. 1845, p. 72.—4. CAYLEY. Davidson's *Hygiene and Diseases of Warm Climates*, Edin. 1893, p. 615.—5. CHAUFFARD. Charcot's *Traité de méd.* t. iii. Paris, 1892.—6. CONWELL. *A Treatise on Functional and Structural Changes of the Liver*, Lond. 1835, p. 72.—7. DE CASTRO. *Des abcès du foie.* Paris, 1870—8. DRAGO. *Arch.*

de méd. nav. 1890.—9. FAYRER, Sir J. *Tropical Diseases*, p 204.—10. FLÜGGE *Micro-organisms*, Syd. Soc. 1890, p. 751.—11. GRAVES. *Clin Med.* lect. liii 12 HASPEL *Malad. de l'Algérie.* Paris, 1850.—13. HIRSCH. *Handbook Geo. and Hist. Path* Lond 1886, vol. iii. p. 412.—14. KARTULIS. *Archiv f. path. Anat. u. Phys.* T. cxviii.—15. KELSCH and KIENER. *Maladies des pays chauds*, Paris, 1889, p. 285.—16. *Ibid.* p. 209—17. MACFADYEN. Davidson's *Hyg. and Dis. of Warm Climates*, Edin. 1893, p. 660—18. MACNAMARA, F. N. *Ind. Ann of Med.* 1862. 19. MACNAUGHT. *Cyclop. Anat. and Phys.* vol. iii. p. 190.—20. MARSTON. *Med. Times*, Sept. 1856.—21. ROUIS. *Sur les suppurations endém. du foie*, Paris, 1860, p. 203.—22. PACHS. *Archiv f. klin. Chir.* Berlin, 1867.—23. THIERFELDER. *Ziemssen's Cyclop.* vol. ix. p. 111.—24. WARING. *Enquiry into the Stat. and Path. of Abscess in the Liver*, Trevandrum, 1851, p. 1[illegible]4.—25. *Ibid.* p. 137.

A. D

AMŒBIC ABSCESS OF THE LIVER

Definition.—Abscess of the liver, single or multiple, occurring in association with dysenteric ulceration of the bowel, active or latent, in which the amœba coli is found bearing a relation to the hepatic lesions analogous to that which it bears to the intestinal lesions.

Etiology.—In 1887, Kartulis of Alexandria described the occurrence of living motile *amœbæ* in the contents of an hepatic abscess. He had already noted their presence in sections of the walls of such abscesses in certain fatal cases of dysentery, in the stools and in the dysenteric ulcers of which the same organism was also present. These observations have been repeatedly confirmed in America by Osler, Councilman and Lafleur, Musser and others; and more recently in Egypt by Kruse and Pasquale, in their extended investigation of amœbic enteritis and hepatitis. [*Vide* art. on "Amœbic Dysentery," vol. ii. p. 753.]

In abscesses involving the liver and lung, which discharge themselves spontaneously through the air-passages, the amœbæ are found in the sputum also (Councilman and Lafleur).

A detailed description of the amœba has already been given in another portion of this work, to which reference may be made [*vide* art. "Amœbic Dysentery," vol. ii. p. 754].

The amœbæ found in abscesses of the liver and lung differ in no essential respect from those present in the stools and in the intestinal lesions of this form of dysentery.

The *bacteria* associated in the lesions with the amœbæ are many. Of thirteen cases of dysenteric liver abscess, examined bacteriologically by Kartulis, the staphylococcus aureus was found in two, and the staphylococcus albus, bacillus pyogenes fœtidus, and the proteus vulgaris in one case each. The remaining eight cases were sterile in this respect. The sterility of the pus is explained by Kartulis on the supposition that the bacteria in closed abscesses of long standing are not so resistant as the amœbæ and quickly perish. Kartulis adopts the classification of tropical liver abscesses into "idiopathic"[1] (those due to bacterial infection from the gastro-intestinal tract) and dysenteric (those due to infection of the liver through the portal system by the intervention of amœbæ which contain bacteria—microbenhaltigen).

Kruse and Pasquale investigated fifteen cases of abscess of the liver, of which nine were idiopathic, and six in association with dysenteric ulceration of the bowels. Amœbæ were found in the latter, but not in the former. In the idiopathic abscesses bacteria were found by cultivation in six cases, and in the dysenteric abscesses in five. Of the various species of bacteria, streptococci were found in three dysenteric abscesses and in one idiopathic abscess, staphylococci in two dysenteric abscesses and in one idiopathic abscess; bacilli resembling that of typhoid fever in four abscesses of both sorts; the bacillus pyocyaneus in three idiopathic abscesses. None of these organisms was found in large numbers except the bacillus pyocyaneus. Councilman and Lafleur in two cases of dysenteric abscess found the Bacillus coli communis in one, and no bacteria in the other. Pansini (quoted by Kruse and Pasquale) obtained typhoid-like bacilli in three dysenteric abscesses.

The relative importance of the amœbæ and of the several other micro-organisms in the production of the lesions in the liver has been variously estimated by different observers. Kartulis considers that the amœbæ play the principal, but not the sole part; that they serve as the vehicles of the bacteria, which may then complete the morbid process; that by their active movements the amœbæ cause rupture of the capillaries, but that the bacteria which accompany them are the pus-producing agents. He does not believe that the amœbæ alone are capable of causing suppuration in the liver.

Kruse and Pasquale lean to the opinion that none of the bacteria found is sufficiently constant to be considered specific; but, nevertheless, that the bacteria cannot be considered as absolutely non-pathogenetic, for all of them can be experimentally shown to possess pathogenetic properties; some of them are the common pyogenetic organisms. They believe in a direct co-operation of the amœbæ with the bacteria in the process of disintegration of the liver tissue and pus-formation.

Councilman and Lafleur think that the amœbæ alone are the active agents in the production of the abscesses. In the smallest abscesses, in which the lesions can best be studied in their inception, they found no bacteria, but the amœbæ were always many. Again, even in the larger abscesses examined by them, the bacteria were not numerous, and the lesions in the liver were in general of a different character from those produced by bacteria. [*Vide* section on pathological anatomy.]

It may be said, at least, that in the idiopathic abscesses—that is, in those which are not accompanied, preceded, or followed by dysentery—no amœbæ, but various forms of bacteria only are found; while in the dysenteric cases—that is, those in which there is either an actual dysentery with amœbæ in the stools, or a history of such an attack—amœbæ are constantly present, and may or may not be accompanied by small numbers of bacteria similar to those found in the idiopathic cases.

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[1] The word idiopathic is one which I do not readily take into use. In the present article, however, it may be serviceable if accepted only in its negative bearings.—ED.

In all the recorded cases amœbic abscess of the liver has arisen secondarily to an attack of amœbic dysentery. It is not necessary, however, that the dysenteric ulceration of the bowel should be active, or even that any dysenteric symptoms should coincide with the abscess: on the contrary, the dysenteric process in the bowel may be latent and, until disclosed post-mortem, even unsuspected.

Whether an amœbic abscess can form in the liver independently of any intestinal lesion is a question that is still undecided. There is no recorded case which may be accepted without reserve as evidence on this point. Kruse and Pasquale mention two cases, but admit that they are not conclusive. In one there were slaty-pigmented scars in the large bowel, suggestive of prior dysenteric ulceration; in the other were ulcers in the stage of healing, though the patient had not suffered from dysentery until after the development of the abscess in the liver. The latter case is undoubtedly an example of latent amœbic dysentery, with exacerbation following abscess-formation; and can in no wise be adduced as evidence of primary amœbic abscess. It is possible, indeed, to suppose a primary infection of the liver through the bile passages, but there is no recorded example of such an occurrence. Amœbic abscess of the liver must, for the present, be considered as invariably secondary to active or latent amœbic dysentery, or, in other words, as a complication of this disease.

With the so-called idiopathic—non-amœbic—abscesses the case is entirely different. Such abscesses usually, if not always, appear independently of intestinal affection, and are not followed by it.

To explain their occurrence one must take into account the general etiological factors that dispose persons in the tropics to inflammatory diseases of the viscera in general, and of the liver in particular. It does not seem probable that these factors can of themselves cause suppuration, but rather that they prepare the tissues for the invasion of one or more species of the ordinary pyogenetic micro-organisms. Through what portals these micro-organisms gain access to the liver is not quite clear, though in a few cases Kartulis has found lesions in the mucous membrane of the stomach.

To discuss whether tropical liver abscess in general is or is not dependent upon dysenteric ulceration of the intestines appears to me to be futile. The intimate association of abscess of the liver with one form of dysentery is quite clear; and what is needed is a more accurate etiological investigation to determine in individual cases which are of dysenteric and which of non-dysenteric (idiopathic) origin. Whether, as a rule, the dysenteric liver abscesses are produced by amœbæ, or whether in tropical countries there are dysenteries, commonly followed by liver abscesses, which are due to some other agent, are also questions that invite further investigation.

The amœbæ found in liver abscesses come from the large intestine, and must necessarily gain access to the liver by way of the blood, by way of the lymph-channels, or by way of the peritoneum. Infection through the bile passages has already been referred to as an hypothetical but not very probable occurrence.

In the case of multiple abscesses in the interior of the liver, it is probable that the amœbæ reach the liver through the radicles of the portal vein. They are often found in the capillaries about the base and sides of the intestinal ulcers. Again, it is possible that secondary abscesses in the liver may be produced by a backward infection of the portal veins from a primary single abscess (Kruse and Pasquale).

Though amœbæ are very often found in the lymph spaces and lymph capillaries of the intestine, it is not probable that infection occurs through the lymph-channels, for before reaching their destination the amœbæ would have to pass through a long series of intervening lymphatic glands and channels; they are very rarely found in any of these glands, nor do the glands present any changes characteristic of the action of amœbæ.

Infection by way of the peritoneal cavity undoubtedly occurs. In one case there was found peritonitis with amœbæ in the exudation over the intestinal coils and the surface of the liver (Councilman and Lafleur). Such a mode of infection explains in a satisfactory manner the frequent situation of the abscesses at the extreme upper portion of the right lobe close to the diaphragmatic attachment, and the early extension of the mischief to the lower lobe of the right lung. It also explains the occurrence of the multiple superficial abscesses, and of abscesses of the under surface of the liver adjacent to the hepatic flexure of the colon.

It is difficult to form an estimate of the frequency of amœbic abscess, for the statistics in which this etiological factor is taken into account are as yet too scanty. Kartulis states that of some 500 liver abscesses which had come under his observation, 55-60 per cent were of dysenteric origin; but he does not state the proportion of cases of dysentery in which abscess supervened. Kruse and Pasquale found abscess six times in 57 cases of amœbic dysentery, and Councilman and Lafleur six times in 15 cases.

The extensive statistics of British and French physicians relating to dysentery and liver abscess in India and other eastern countries are not directly available for purposes of comparison, as no mention is made of the etiological factor, and the various kinds of abscess are not distinguished. It is highly suggestive, however, that the collective statistics of liver abscess and dysentery in the tropics show an average of one case of liver abscess for every four or five cases of dysentery. These figures lend a probability to the supposition that a large proportion of the cases were of amœbic origin, for it cannot be questioned that in the diphtheritic and in catarrhal dysenteries of temperate climates abscess of the liver is a rare complication.

Pathological anatomy.—(*a*) *Lesions in the liver.*—Leaving the abscesses out of account, the liver is generally of normal size, sometimes enlarged:

in some cases it is congested, in others pale. There are areas of local peritonitis where the larger abscesses reach the surface of the liver, and when an abscess is situated in the uppermost part of the right lobe close to the diaphragm, the latter is bound to the liver over the periphery of the abscess by very dense adhesions. *The abscesses may be one or more: in the latter case there is usually one which is larger and evidently* of longer standing than the others. Sometimes, in the same liver, abscesses of all ages are to be seen, from the smallest and most recent with no definite walls to the oldest with dense fibrous walls. The smallest visible abscesses are from 1 to 5 mm. in diameter; the largest may attain the size of a large orange or even, in rare cases, of an infant's head.

As a rule the right lobe of the liver is the seat of the large abscesses, and certain portions of the lobe are especially prone to be affected, namely, the under surface adjacent to the hepatic flexure of the colon, and the dome of the liver close to the diaphragmatic attachment. The small multiple abscesses are commonly superficial, or at any rate near the surface; but in a few instances they are found scattered throughout both lobes of the liver.

The general shape of the abscesses is spherical or ovoid, but there are often irregularities in outline, especially in the larger ones, due to unequal extension in different directions.

With regard to the naked-eye appearance the abscesses may be divided roughly into three varieties: small, very recent abscesses; abscesses of larger volume, with walls partly necrotic and partly fibrous, which are evidently still extending, and old abscesses, apparently stationary, with firm and thick fibrous walls.

The contents vary with the kind of abscess. In the smallest they can scarcely be called fluid, for they do not empty themselves on section; a little glairy translucent fluid exudes, leaving a yellowish-gray spongy mass behind. In the larger and older abscesses the contents are more liquid, of a grayish, a yellowish-gray, or a mottled yellowish-red or brownish-red colour (which indicates admixture of blood), and frequently numerous yellowish or grayish shreddy fragments of necrotic liver tissue are mixed with the more fluid portions. Even in these larger abscesses the contents are very viscid, and do not resemble ordinary pus.

Under the microscope the contents of the abscesses are seen to consist mainly of a finely granular detritus, containing fragments of cells, a few leucocytes and red blood corpuscles, hæmatoidin crystals, necrotic or fattily degenerated liver-cells, and amœbæ which, if the autopsy had been performed a few hours after death, will still exhibit active movements. The amœbæ are most numerous and active in the very small abscesses.

Bacteria are very sparingly found in cover-glass preparations, and at times only by cultivation in suitable media. The species found have already been stated.

The absence of large numbers of leucocytes, such as constitute the bulk of the cellular elements in ordinary pus, is especially noteworthy.

When the contents are removed it is seen that the walls of the *abscesses are irregular, and covered with a dirty, grayish-yellow necrotic* shreddy material, which extends to a variable distance into the liver. This is more marked in medium-sized and rapidly extending abscesses than in the older ones. The latter may have smooth well-defined fibrous walls, with fragments only of necrotic liver tissue adhering to them here and there. The fibrous wall varies very much in thickness; in some instances it is more than a centimetre thick, and is of a firmness almost cartilaginous. In the smallest abscesses there is often no definite wall at all, the necrotic tissue passing insensibly into normal liver tissue.

The pathological histology and mode of formation are best studied in the smallest abscesses, as sections can be made including the whole of the abscess and a portion of the surrounding tissue. Hardening in alcohol and staining with methylene blue is most useful for general purposes; for more minute study Flemming's solution, followed by deep staining with safranin, is the best. In sections so treated the abscess contents are pale and finally granular with small brightly-stained particles, the result of nuclear fragmentation. There are present also darkly-stained circumscribed masses, some of which are isolated and others connected with the wall of the abscess; these are fragments of liver which have resisted the process of disintegration, and are composed of fibrous connective tissue with areas of round-cell infiltration. They contain an artery, a vein, and one or more bile-ducts, the latter being lined with low cuboidal epithelium, and thus resembling newly-formed bile-channels. Around these vessels are liver-cells more or less necrotic. It is evident from their histological structure that these masses are remains of the portal system of the liver. A study of the periphery of the small abscesses shows that the interlobular areas are always the first to become disintegrated; and to this process is due the irregular contour of the abscess wall, the periportal areas persisting until they are detached from the wall by the confluence of the foci of interlobular necrosis.

In addition to finely granular detritus, and the fragments of liver tissue above mentioned, the abscess contains a few red blood corpuscles and leucocytes, fibrin filaments, and necrotic liver-cells. The latter are often elongated, with pointed ends, or they may be of irregular shape and contain vacuoles. They refract light more than normal liver-cells, and contain no nucleus.

In the foci of necrosis around the abscess cavity the capillaries are dilated and filled with blood or, when near the cavity, with granular contents like the abscess. There is a dissociation of the capillary wall from the trabeculæ of liver-cells, and the latter are thinned, highly refractive, and vacuolated, many of the vacuoles containing fat. A peculiar refractive reticulum, similar to that found at the bases of the intestinal ulcers, is often seen around the borders of the abscess and the isolated fragments of periportal tissue.

In most instances there is no accumulation of leucocytes either in the necrotic tissue or in the capillaries. This absence of inflammatory *reaction on the part of the tissue is characteristic of amœbic abscess.*

Numerous amœbæ are found in the tissues, chiefly in the periphery of the abscess, where they occupy the capillaries, and around the portal tissue fragments. They are but seldom found beyond the zone of necrosis.

The larger chronic abscesses present some differences in structure from that of the small abscesses—differences that are explicable on the supposition that the amœbæ are fewer in number, and that the necrosis of the liver tissue is less diffuse. They usually have a definite wall of connective tissue. Sections of this wall show at the innermost part more or less granular necrotic material, beyond this the refractive reticulum mentioned above, then a zone of granulation tissue of varying width composed of uninuclear round cells, and, finally, a zone of fibrous connective tissue which contains spindle-shaped cells and small-celled infiltration both diffuse and circumscribed. In the connective tissue zone, which is highly vascular, there are numerous, often branching, bile-ducts. In the outermost part of this zone liver-cells are found, singly or in groups of two or three at first, then in larger agglomerations. They are much swollen and fatty, but still possess a nucleus. Still further outward in the liver tissue, which shows strands of connective tissue rich in round cells, the capillaries are engorged and small hæmorrhages are common. When the abscess is large there is evidence of pressure, the adjoining liver-cells for a considerable distance being flattened and spindle-shaped. Amœbæ are much less numerous in the chronic abscesses than in the small acute ones, but are found chiefly in the same situation, that is, in the necrotic zone of the abscess just at the edge of the round-celled infiltration. In the connective tissue zone they are scanty and occupy the blood-vessels and the spaces of the tissue.

Abscesses of the under surface of the liver, which are connected with the bowel, more frequently show a true purulent infiltration of the tissues, owing to the invasion of pyogenetic bacteria; the conditions being analogous to what is seen in some of the intestinal ulcers where there is a mixed infection.

In addition to the formation of abscesses there is another very important change in the liver, which consists in a widespread necrosis of the cells around the central vein of the lobules, and is most marked in the vicinity of the abscesses but is not confined to such parts. These foci of necrosis never contain amœbæ, and, as they are not the result of pressure or of a local anæmia, the most plausible explanation of their occurrence is to assume that the amœbæ produce some soluble toxic substance that induces these changes. Though not due to the direct agency of the amœbæ the necrotic areas are more vulnerable than the rest of the tissue, and it is by the softening of these patches that the abscesses extend.

The changes in the liver may be summed up as follows:—1st, a widespread necrosis of the liver-cells, due most probably to soluble chemical products of the amœbæ; and, 2nd, the formation of abscesses, due to the direct action of the amœbæ, which cause disintegration and liquefaction of the necrotic tissue. It is to be particularly noted that reaction on the part of the tissues in the form of suppuration—leucocytic infiltration of the tissues, and the presence of leucocytes in the abscess contents—is as a rule absent, there being no more leucocytes found than those normally present in the vessels of the tissue involved in the abscess.

(*b*) *Lesions in the lung.*—Abscess of the lung is always secondary, and arises by the direct extension through the diaphragm of an abscess at the extreme upper portion of the right lobe of the liver. The abscesses *are never metastatic, and it is always the lower lobe of the right lung that is involved.* The diaphragm is intimately adherent to the surface of the liver, and usually also to the under surface of the lung; but in some instances a collection of pus in the pleural sac separates the diaphragm from the lung. The inferior portion of the lower lobe and often a portion of the middle lobe are consolidated, and there are adhesions between them and the parietes.

On section an abscess cavity is disclosed in the interior of the consolidated portions, extending from the diaphragm to a variable point upwards, but not usually reaching the surface of the lobe. It is thus centrally situated in the base of the right lung. There is usually an opening in the diaphragm, but of smaller size than the diameter of either the hepatic or the pulmonary abscess. In some instances the diaphragm, though much thickened, shows no visible solution of continuity.

The consolidated lung tissue adjoining the abscess is very dense, of a whitish opaque colour near the abscess, grayish and translucent beyond. The cut surface is quite smooth and œdematous.

The bronchi contain either a purulent or a serous fluid.

The abscess cavity may or may not be empty, according as there has or has not been evacuation through the bronchi. As in the hepatic abscess, the contents consist of a viscid yellowish-gray or yellowish-red fluid, which does not resemble ordinary pus, and contains numerous shreddy necrotic fragments. Under the microscope are seen granular detritus, round lymphoid cells, some leucocytes, many red blood corpuscles, fat globules, amœbæ, and elastic tissue fibres from the lung.

The walls of the abscess are even more irregular than those of the hepatic abscess, and are covered with ragged sloughy material, which often projects in tag-like pieces into the abscess cavity. In some places the abscess wall may be smooth and formed of dense connective tissue, and in others soft and œdematous, without a definite fibrous capsule.

Sections of the wall of the abscess show next to the cavity a granular mass containing cellular elements and nuclear fragments. Farther away there are small pieces of lung tissue, chiefly elastic fibres, but sometimes also distinct groups of air-cells, mostly necrosed. Beyond this is the connective tissue zone, which shows round-cell infiltration, and may be quite thick; or where the abscess is extending rapidly there may be no definite fibrous wall, so that the granular necrotic zone extends directly to the lung substance. Both fibrin and the hyaline reticulum above mentioned are found in places at the border of the abscess.

In the portions of the lung adjacent to the abscess the interstitial tissue is much increased at the expense of the alveoli, which are small, of irregular shape, lined with a cuboidal epithelium, and resemble rather glandular than pulmonary tissue. Nuclear figures are frequently seen in these epithelial cells. The alveoli near the abscess are filled with large round fatty cells which bear a close resemblance to amœbæ; they also contain numerous granulation cells and a few leucocytes. The *more distant alveoli contain fibrin, or bud-like projections from the proliferating interstitial tissue.*

The walls of the bronchi are thickened and infiltrated with numerous round cells. Their contents are either pus cells, fibrin, or lymphoid cells.

Amœbæ are found in these abscesses, and are especially numerous where the abscess is extending rapidly. They are present also in great numbers in the alveoli adjoining the abscess; more sparingly in the remoter ones and in the bronchi near the abscess cavity. When present in the fibrous connective tissue zone they occupy the blood-vessels and spaces in the tissue.

In the main, making due allowance for the difference in the tissues affected, the changes produced by the amœbæ in the lung are similar to those seen in the liver—necrosis followed by liquefaction of the tissues; and there is the same absence of the products of suppurative inflammation.

(*c*) *Lesions of the peritoneum.*—Peritonitis, local or general, is sometimes found. It is fibrinous, the exudation being pale and translucent, and containing a good deal of fluid. The cellular elements found in the exudation are lymphoid cells, a few leucocytes perhaps of other kinds, and cells from the endothelium with oval nuclei in great numbers. Amœbæ were present in two out of three cases.

Symptomatology.—Amœbic abscess of the liver may seem to occur as a primary condition without any evident disturbance of the intestinal tract, or again as a complication of a well-marked dysentery at some period of its course. The latter case is the more frequent. Even in the former case the independence of the hepatic condition is more apparent than real, for by careful inquiry a history of some trivial diarrhœa, occurring, it may be, weeks or even months before the unequivocal signs of abscess-formation in the liver, is often elicited; and examination of the formed stools in such cases may show actively motile amœbæ. Moreover, that dysenteric ulceration may be latent—that is, unaccompanied by any symptoms or signs pointing to ulceration of the bowel—is amply proved by the discovery of unhealed intestinal ulcers in patients who have suffered during life from suppurative hepatitis apparently primary.

Whether apparently primary, or associated with an undoubted dysenteric attack, the course of the illness is practically the same in both cases. The onset is insidious, and, as a rule, owing to the usually deep-seated position of the abscess, the first indications of the implication of the liver are derived from the subjective rather than from the physical signs. When abscess occurs in the course of a dysentery of moderate severity it is usually at some date between the fourth and twelfth weeks of the intestinal affection. In chronic dysentery, however, there is no such limitation of time, and abscess may arise after an intestinal flux had persisted for months, or even for years. In gangrenous dysentery death usually occurs before there is time for the liver to become infected.

The illness begins most frequently with pain, fever, and sweating, the pain being usually in the region of the liver, or near the lower part of the scapula. The patient loses appetite, emaciates more or less rapidly, and becomes progressively weaker and more anæmic. The skin assumes a moderate icteroid hue, but pronounced jaundice is not common There is sometimes much gastric distress with attacks of vomiting, but hiccough is more usual. On the whole, the general features of the disease are those of septic absorption from an internal focus of suppuration. If the abscess be not evacuated, spontaneously or by surgical intervention, death occurs sooner or later from exhaustion.

In a considerable number of cases there are symptoms pointing to the extension of the disease to the lower lobe of the right lung. It is certain that implication of the lung is more frequent in amœbic abscess than in abscess due to other causes, whether of dysenteric origin or not; and this is attributable to the frequent situation of such abscesses at the extreme upper part of the right lobe of the liver. In such cases symptoms of pulmonary disease are apt to occur early and to predominate throughout the illness; the clinical picture, indeed, is often rather one of a destructive lesion of the lung than of hepatic suppuration. (A well-marked example of this condition is seen in the case illustrative of Amœbic Dysentery given in vol. ii. of this work, p. 769.) The chief symptoms are early stitch-like pains in the right side of the chest, dyspnœa, and cough, at first hacking and ineffectual, but later, when the abscess is evacuated through the bronchi, paroxysmal, and accompanied by muco-purulent blood-stained expectoration containing amœbæ. Abscesses of this course show little tendency to heal, and in my experience they progress as a rule to a fatal termination, notwithstanding the seemingly free evacuation of the abscess cavity. Recovery may ensue after the patient has been spitting muco-pus for weeks or even months, but convalescence is very tedious and may be interrupted by exacerbations of the cough and expectoration.

The duration of fatal cases is about two or three months.

With the progress of both hepatic and hepato-pulmonary abscess there is either an aggravation of an existing dysentery, or this condition makes its appearance; even in cases in which the hepatitis appeared to be primary.

Analysis of symptoms.—*Pain* is one of the earliest symptoms; it occurs at some period of the illness in all cases. It may be dull and aching, or sharp, lancinating and tearing in character. The former kind of pain is usually felt earlier, and is possibly due to the distension of the liver by the abscess contents: the latter in all probability indicates implication of the peritoneum—visceral or parietal—or of the pleura, and is certainly more frequent and more severe in those cases in which the lung becomes involved. In the latter case it is aggravated when the patient breathes deeply, and during paroxysms of cough. The pain is modified by the movements and position of the patient, the easiest decubitus being the right dorso-lateral, with the body slightly raised and the thighs flexed. The site of the pain varies in different cases. It may be in the epigastrium, the right hypochondrium, or the lower axillary space; posteriorly it is usually referred to the right scapular region, or to the shoulder-joint itself. From any one of these points it not infrequently radiates with increasing intensity over the whole of the right side of the chest and the upper abdominal zone. Discharge of the abscess, by surgical intervention or by evacuation through the bronchial channels, is followed by an abatement of the suffering.

Fever of an irregular remittent or intermittent course is the rule in amœbic abscess. The pyrexia does not differ widely from that observed in cases of dysentery uncomplicated by abscess; but the range is higher, varying between 100° and 103° F., and the remissions are more pronounced. The remission usually occurs in the morning hours, the exacerbation towards evening; but a reversed temperature curve may be seen occasionally, as in other diseases characterised by a septic temperature curve.

At the earliest period of abscess-formation the prevailing fever is continuous, or slightly remittent; but, as the infection progresses, the remissions become greater, and ultimately complete intermissions occur at some time in the twenty-four hours.

The temperature falls when the abscess is evacuated, through the bronchial tubes or otherwise; but irregular fever may persist until the abscess cavity is completely healed.

Sweating is invariably present, and is often profuse and drenching. It does not appear to be more frequent at night than during the day, it is very irregular in its occurrence, and is independent of the course of the temperature. In any case of amœbic dysentery the appearance of this symptom should at once suggest infection of the liver; for as a rule the skin in dysentery uncomplicated by liver abscess is dry and rough. An exception may be made in the gangrenous form, but even then only in the later stages. Moreover, in these cases it is rather a continual clamminess of the skin than periodical and profuse sweating. There is not often a definite rigor, but a chilly feeling before and after the sweating is not uncommon.

The *pulse* and *respirations* are both accelerated. In the earlier stages the pulse ranges from 80 to 100, and has the usual characters observed in febrile affections, being full and regular. Towards the end of fatal cases it becomes rapid, from 120 to 140, small and easily compressible. The respirations are increased most obviously in the cases of hepato-pulmonary abscess, and may range from 24 to 40. The breathing is often more rapid and shallow at the beginning of the lung infection than at a later period of the disease. This is due to the pleurisy that in every case precedes the extension of the process into the lung itself. In fact the attitude of the patient, and the character of the cough, the pain, and the breathing, immediately suggest this event.

When a purulent effusion takes place, or the pleural surfaces become adherent—and this is the more frequent result—the dyspnœa is much less, and is still further relieved by a free evacuation of the abscess contents through the bronchi.

In hepato-pulmonary abscess *cough* and *expectoration* are constant and often very distressing symptoms. During the earlier part of the illness —that is, before any definite physical signs in the lung—the cough is frequent, hacking, and usually accompanied by pain in the right side, right hypochondrium, or epigastrium. It suggests diaphragmatic pleurisy, and is no doubt due to it. At this stage there is either no expectoration, or a scanty clear mucoid or muco-purulent sputum, occasionally tinged or streaked with blood. Then after a variable lapse of time the cough becomes more severe and paroxysmal, and during one of these paroxysms the patient brings up a large quantity of reddish or reddish-brown muco-pus, sometimes mixed with pure blood. This usually gives a good deal of relief for a time, and the paroxysms of cough become less severe and frequent. The sputum in such cases was described many years ago by Budd, and was considered by him to be characteristic of the disease. "When this happens (evacuation of an hepatic abscess through the bronchi), it is marked by the sudden expectoration of a dirty red or brownish puriform matter. The peculiar colour arises from the pus in its passage through the lung becoming mixed with blood and broken-down pulmonary tissue. There is no matter like it expectorated in any disease of the lung itself, and I believe that its appearance is pathognomonic of abscess of the liver, or at least of abscess perforating the lung. I have been led by it to detect an abscess of the liver, of which I had previously no suspicion."

The following description of the sputum in cases of hepato-pulmonary abscess, given by myself some time ago, may be quoted here in illustration of those cases in which amœbæ are present:—"The expectoration is partly diffluent, partly tenacious, and partly frothy, its viscidity being proportional to the amount of mucus present. It is at first often bright red owing to a large admixture of blood, and subsequently of a dull brick-red, brownish-red, or rusty brown colour, and occasionally bile-stained. Intimately mixed with the muco-purulent mass are more or less numerous small yellowish-white fragments of a friable or cheesy consistency. After exposure to air for some time the whole mass liquefies into a thin syrupy or oily homogeneous fluid, which has frequently been compared to anchovy sauce. Such a fluid was aspirated from an abscess of the liver which had not perforated the lung. The sputa are alkaline in reaction, and have a faint sweetish odour. At a later period they become more purulent, sometimes nummular, reddish-yellow, and contain less blood. If the patient progress toward recovery, the expectoration becomes more fluid and frothy, and contains less pus, which is slightly blood-stained. On settling, it separates into an upper frothy layer, a middle layer of slightly turbid fluid, and a thin bottom layer of muco-pus. The quantity expectorated daily varies from 25 c.c. to 400 or 500 c.c. Even more than this may be coughed up at the time the abscess first discharges itself.

"*Microscopical characters.*—The cellular elements observed are red blood corpuscles, leucocytes, round alveolar epithelial cells, oral epithelium, and irregular polyhedral fatty degenerated elements, which look like liver-cells, but do not show a nucleus. In the early sputa red blood corpuscles predominate, and in the later sputa leucocytes; while swollen and degenerated alveolar epithelium is present in about the same proportion in all the sputa. Elastic tissue fibres from the lung, single or in groups, showing the characteristic wavy or curled appearance, are frequently found, more especially in the later stages. Orange-red rhombic crystals of hæmatoidin, needle-shaped crystals of tyrosin, single or in fan-shaped groups of the same colour, and Charcot's crystals, are occasionally seen, with various bacteria and particles of food. The small cheesy fragments consist entirely of an amorphous granular material and oil globules. Amœbæ are constantly present. They occur indifferently in all portions of the expectoration more or less abundantly, but on the whole they are not so plentiful as in the stools. The number observed from day to day is very variable. They vary in size and activity, but are generally larger than those seen in the stools, and very frequently contain red blood corpuscles. For their detection the same precautions should be taken as in the case of the stools, that is, the sputa should be kept at a temperature of 30° to 35° C., and examined as soon as possible."

Disturbance of the gastro-alimentary tract is apt to occur with abscess of the liver. The most constant and persistent symptom is *anorexia*, which is often absolute, even the blandest food being distasteful. On the other hand, thirst is increased, owing to the drain of the tissue fluids caused by the profuse and recurring sweating.

Nausea and vomiting occur in those cases in which the lung becomes engaged, and are induced chiefly by the violent fits of coughing. When the lung is not engaged these symptoms are not frequent or severe.

Jaundice is occasionally present, but the hue is not deep as in the obstructive icterus; it is rather an aggravation of the sallow icteroid tint seen in cases uncomplicated by liver abscess, and the stools still contain bile pigment.

Physical signs of hepatic and hepato-pulmonary abscess.—(*a*) The physical signs of an *hepatic abscess* develop slowly, and for a time are often obscure and inconclusive. If the abscess occupy the left lobe or the anterior and lower part of the right lobe, direct evidence of its presence occurs earlier than if it be situated centrally in the right lobe, or toward the convexity of the liver.

Inspection affords no clue until the abscess has reached considerable dimensions. When this is the case the lower ribs and cartilages on the right side may be more prominent than those on the left, and the expansion of the right lower thoracic zone is diminished. The epigastric hollow may be obliterated, and the costal margin on the right side indistinguishable. Very seldom is there any obliteration, still less any bulging of the lower intercostal spaces.

The measurement of the thorax below the mammilla sometimes shows the right side of the chest to be larger than the left.

The edge of the liver is often palpable below the costal margin, and to a lower point than usual in the epigastrium; but as there is often sensitiveness to pressure in these situations, it may be impossible properly to carry out the manipulations necessary for this investigation. Sensitiveness to pressure may occasionally be elicited also by firm palpation over the lower ribs and cartilages. When the abscess points *towards the abdominal wall it may be possible to feel an irregularity in the outline of the hepatic margin, and sometimes to detect deep fluctuation*, especially if the abscess be in the left lobe.

Percussion of the hepatic area usually affords the first definite evidence (in conjunction with the rational signs) of amœbic abscess. The zone of liver dulness is enlarged, the direction and degree of the enlargement depending upon the seat and the size of the abscess. With abscess of the left lobe, or of the anterior portion of the right lobe, the liver dulness is increased chiefly downward; while an extension of the upper margin of liver dulness is observed when the abscess occupies the centre of the right lobe, and more especially the dome of the liver close to the diaphragmatic attachment. In the latter case, however, the physical signs are usually very indefinite, and are late in appearing.

Auscultation reveals nothing if the abscess involve the liver alone, unless, indeed, it be of very considerable size, and encroach upon the area of normal pulmonary sounds, which are then enfeebled to a corresponding degree. Occasionally a peritoneal rub may be heard over the lower ribs and cartilages anteriorly.

(*b*) In *hepato-pulmonary abscess* the physical signs are at first even more indefinite, and may remain so for a longer time than in hepatic abscess. It is surprising in some cases to find extensive lesions of the liver and lung after death, where physical examination (including exploratory aspiration) had afforded but inconclusive evidence of suppuration in these organs.

The deep situation of the lesions, and the comparatively early evacuation of the abscess contents through the bronchi, are answerable for this discrepancy; though, it may be added, the rational signs in all such cases are sufficiently suggestive, if not conclusive.

Although the liver is in every case affected before the lung, it is in the latter, as a rule, that the first definite physical signs are found.

Very little information is elicited by inspection and palpation. The *expansion of the right side of the chest is less marked than that of the left, but bulging or enlargement of the right lower thoracic zone is* either not seen at all, or only at an advanced stage of the illness. Friction fremitus may occasionally be felt in the lower mammary or axillary areas, and some tenderness is elicited by firm pressure in the same situation and below the margin of the ribs, or in the right epigastrium.

On percussion there is noted a gradual increase in the area of hepatic dulness, chiefly upwards, the area of lung resonance being correspondingly decreased. There is also an extension of liver dulness in the abdomen, but this appears later and is not so pronounced as the upward extension, which may reach the fifth or even the fourth rib in the mammary line, and extend posteriorly to a point considerably above the inferior angle of the scapula. Above the hepatic dulness there is a more or less well-marked zone of high-pitched or even sub-tympanitic resonance (collapse of lung), which passes insensibly into normal pulmonary resonance above.

On auscultation it is found that the breath-sounds at the base of the right lung, in the lower axillary space and below the nipple are almost inaudible or entirely absent. Over the zone of the high-pitched or sub-tympanitic resonance they are enfeebled, have a faintly bronchial character, more especially behind between the scapula and the vertebral column, and are accompanied on inspiration by muffled crackling râles, particularly in the interscapular region. A friction rub may be heard in the lower mammary and axillary spaces. Vocal resonance is slightly diminished, and the voice has a nasal quality. Over the upper portion of the lung the respiratory murmur is enfeebled, but not altered in quality.

On the whole the physical signs have a close resemblance to those found in limited pleural effusions.

A marked change in these physical signs is observed when the abscess has emptied itself through the air-passages. The edge of the liver may now no longer be felt below the costal margin, and the area of hepatic dulness is less than before: the change being most evident in the mammary and axillary areas. Over the zone of high-pitched resonance the respiratory murmur has become frankly tubular, especially about the inferior angle of the scapula and the posterior axillary space; and coarse bubbling or even gurgling râles are heard on inspiration and coughing. These râles have the consonating quality which is characteristic of cavity formation. Vocal resonance is now increased over this zone, and the voice-sounds are articulate and nasal. The whispering voice may be distinctly heard, usually most intensely in the lower interscapular space.

The above signs gradually disappear if recovery follows; but an enfeebled respiratory murmur, with more or less numerous crackling râles at the base of the right lung, may persist for many weeks.

Diagnosis.—The diagnosis of amœbic hepatic or hepato-pulmonary abscess is based on a history of a previous or actual attack of amœbic dysentery, and on the rational and physical signs of abscess-formation in the liver and lung. The stools should be carefully examined for amœbæ.

If there be diarrhœa, these are readily found; but when the stools are formed, as sometimes happens, there is some difficulty in detecting them. In the latter case the mucus adhering to the fæces may contain a few amœbæ.

Sometimes the amœbic nature of the abscess is first demonstrated by finding actively motile amœbæ in the sputum when the abscess has evacuated itself through the bronchi.

Definite information may also be obtained, before spontaneous evacuation, by exploratory puncture of the liver with a long and large-sized aspirating needle. I have often been disappointed, however, in this procedure, even when the physical and rational signs were apparently quite conclusive. Failure to obtain pus is usually due to the deep situation of the abscess and to the great viscidity of the contents of it. Exploratory aspiration, if unsuccessful at first, should be repeated from time to time, a different portion of the dull zone being selected each time; in this way a positive result may be obtained, and if amœbæ are found in the material withdrawn the diagnosis is established.

It is practically impossible to diagnose multiple abscesses, or a small abscess in the concavity of the liver due to direct infection from the hepatic flexure of the colon.

The only diseases that are likely to be mistaken for amœbic abscess are non-amœbic liver abscess, pyæmic abscess, sub-diaphragmatic abscess, empyæma, and possibly basic tuberculosis of the right lung. In non-amœbic abscess there is very often no history of any intestinal disorder, and the abscess appears to be idiopathic. Moreover, the abscess is usually large and single, and an exploratory puncture readily affords a rather thin pus which contains no amœbæ but usually one or more species of the pyogenetic cocci. The pus may, however, be entirely sterile, and in such cases the disease pursues a much more benign course than is the rule with amœbic abscess. There is not the same tendency to implication of the lung in non-amœbic as in amœbic abscess.

Pyæmic abscess, which is usually multiple, is distinguished by its more rapidly fatal course, and can generally be traced to some localised abdominal or pelvic focus of suppuration.

In the case of the three other conditions mentioned which may simulate the hepato-pulmonary form of amœbic abscess, an error in diagnosis can occur only before spontaneous evacuation through the bronchi; or when the stools, whether formed or diarrhœal, do not contain amœbæ. After rupture of the abscess amœbæ will invariably be present in the sputa, and the doubt at once dispelled.

Prognosis.—The prognosis of amœbic abscess of the liver, and especially of the liver and lung, is very unfavourable. These sequels are responsible for a large percentage of the mortality from this form of dysentery, and in many cases, both of dysentery of moderate severity and of chronic dysentery, are the final events.

Even when the dysentery is latent, that is when there are no actual intestinal symptoms, the outlook is not very much better; for an exacerbation of the intestinal condition is very apt to occur with the development of the hepatic complication.

Surgical intervention, moreover, is not as a rule followed by such satisfactory results as in the case of non-amoebic abscess. In a series of eleven cases of liver abscess observed in Baltimore, of which seven were of amœbic origin, and four non-amœbic, one of the former and three of the latter ended in recovery. Three of the amœbic cases were operated on, and all died, the only recovery being a case of hepato-pulmonary abscess which emptied itself spontaneously through the bronchi. All the non-amœbic cases were subjected to operation, the result being three recoveries and one death.

Treatment.—Notwithstanding the slender hope of recovery after operation, the treatment of amœbic abscess of the liver and lung must be surgical. The choice and time of operation are questions for the surgeon to decide. It is usual to perform the operation in two stages: the liver is first exposed and sutured to the anterior abdominal wall, and a few days later, when adhesions have formed, an opening into the abscess cavity is made with the thermo-cautery. Free drainage is essential. It is of some advantage to irrigate the cavity with a solution of quinine, which readily destroys the amœbae.

Unfortunately there are often secondary abscesses of small size adjacent to the main abscess which are only discovered after death.

In hepato-pulmonary abscess which is discharging itself spontaneously and freely it is questionable whether surgical intervention is at all likely to advance the recovery of the patient. The abscess is usually so deep-seated, and efficient drainage is so difficult to establish, that unless the physical signs be very definite and localised, it is probably more prudent to abstain from operation.

The medical treatment of abscess of the liver and lung differs in no essential respect from that of the intestinal disease which accompanies and has given rise to these conditions. The chief symptoms requiring the aid of the physician are pain and cough. For the relief of the former morphia, administered preferably by hypodermic injection, is usually required; the latter may be alleviated by the same means or by codeia. When spontaneous rupture through the bronchi has occurred it is well to reserve the use of the morphia for the night-time, in order to secure some rest and not to interfere with the cough necessary to the emptying of the abscess cavity.

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REFERENCES

1. COUNCILMAN and LAFLEUR. "Amœbic Dysentery," *The Johns Hopkins Hospital Reports*, vol. ii. 1891.—2. KARTULIS. "Zur Aetiologie der Leberabscesse; lebende Dysenterie-Amoeben im Eiter der dysenterischen Leberabscesse," *Cent. f. Bakt.* Bd. ii. 1887.—3. *Idem.* "Ueber tropische Leberabscesse und ihr Verhaltniss zur Dysenterie," *Virchow's Archiv*, Bd. cxviii. 1889.—4. KRUSE and PASQUALE. "Untersuchungen uber Dysenterie und Leberabscesse," *Zeitschr. f. Hygiene und Infectionskrankheiten*, Bd. xvi. Hft. 1.

H. A. L.

DISEASES OF LYMPHATIC AND DUCTLESS GLANDS

DISEASES OF THE THYROID GLAND

INTRODUCTORY REMARKS

Physiology.—The structure of the thyroid gland is well known from the descriptions given in the ordinary text-books. It consists of closed vesicles held together in groups or imperfect lobules by areolar tissue. The vesicles vary in size from about 0·03 mm. to 2 mm.; their walls consist of simple layers of cubical or columnar epithelium cells without any basement membrane; their interior is filled with a yellow glairy fluid, the so-called colloid material, and detached epithelium cells. In the periphery of the colloid, vacuoles are to be seen in the vicinity of the more active cells. In the interstitial connective tissue there are plasma cells, and its spaces may be filled, like the vesicles, with colloid material. The blood-vessels and lymphatics reach the vesicles by means of the interstitial tissue. The capillaries are in close contact with the epithelium, and may even project between the cells.

Occasionally incompletely developed portions may here and there be found in which anastomosing cylinders of columnar cells occur.

Special attention has been drawn of recent years to certain bodies, either embedded in the thyroids or external to them, which, while resembling thyroid tissue to the naked eye, are found to present important structural differences from it. These bodies have been called parathyroids, and were originally described by Sandstrom in 1880. They are found in the lower animals as well as in man. In the dog, cat, and rabbit there are usually four of these bodies—two internal lying close to the thyroid, and two external. In man there are usually four external parathyroids, but the number may be larger or smaller. These bodies were originally supposed to consist of embryonic thyroid tissue, which in structure they resemble. They consist mainly of secreting cells arranged more or less in columns separated by capillaries. They, however, contain neither vesicles nor colloid. Here and there may be seen drops of secretion which do not stain darkly as does the colloid in thyroid vesicles. The parathyroids develop in advance of the thyroid itself. This fact, in connection with their resemblance to adult structures, such as the suprarenals and the carotid gland, points to their being adult and not embryonic tissues.

The knowledge we possess of the function of the thyroid gland is of comparatively recent date. That the gland had any important function to perform was not considered likely. Some supposed it was simply a pad to protect the trachea and fill up the contour of the neck. Others imagined that it acted as a kind of safety-valve to the vessels feeding the brain. Sir John Simon suggested that each lobe had a special nutritive relation to the corresponding cerebral hemisphere. The importance of the organ to life and health was first clearly demonstrated by Schiff, in 1884, who found that the removal of the thyroid gland in dogs is almost invariably followed by profound illness and death.

It was next observed that some animals, such as rabbits, bore the removal of the thyroid well; and that sheep and monkeys, although profoundly affected at first, might survive the operation for a considerable time. In some of the animals which survived the operation of removal of the thyroid it was found that accessory thyroids or parathyroids had been left. In the rabbit the external parathyroids are situated on each side of the trachea below and quite apart from the thyroid proper. Hence when the thyroids are removed in these animals, these parathyroids are almost invariably left behind. In the dog, on the other hand, the parathyroids are closely connected with the thyroid, and, as a rule, are removed along with it. These observations suggest that the parathyroids are of great importance, and that their removal is probably the cause of the rapidly fatal result observed constantly in dogs, and sometimes in other animals.

It was therefore important to observe separately the effects of removing first the thyroid, and secondly the parathyroids.

The first experiments on the parathyroids were fallacious, because it was not then recognised that there are internal as well as external parathyroids. Vassale and Generali have recently extirpated the four parathyroid glands in ten cats and nine dogs. Nine of the cats and all the dogs succumbed within ten days, the dogs dying more quickly than the cats. One cat survived six weeks, but was then in a state of cachexia. The removal of two parathyroids, or even of three, appeared to produce only transitory symptoms; but the subsequent removal of the remaining one or two resulted in acute symptoms and death. Apparently the internal and external parathyroids are of equal importance, for it made no difference which were removed first. The experiments of these observers are both numerous and conclusive; but like all investigations of this kind they require confirmation.

The experiments carried out by Edmunds, previous to Vassale and Generali's work, are thoroughly in accordance with their results. He found that if the whole of one lobe of the thyroid of the dog, including the parathyroids, and also the greater part (two-thirds or more) of the other lobe be removed, the animal will live or die according as the parathyroid is or is not left. In the animals which survived, the removal of the remaining parathyroid at a later period, in some cases at an interval of six months after the first operation, was quickly followed by acute illness and death.

The acute symptoms supervening on removal of all the parathyroids in cats and dogs are as follows:—The animal becomes dull and apathetic. It suffers from general muscular weakness. Its gait becomes unsteady.

Tremors and fibrillar twitchings come on. Trismus and rigidity of the posterior limbs show themselves. Attacks of dyspnœa appear. The appetite may be increased at first, but is soon lost. Vomiting, palpitation, scantiness of urine, and sometimes albuminuria are also observed. Slight convulsions appear just before death.

The symptoms observed in the dog on complete removal of the thyroid gland agree with these in every respect; except that convulsions come on earlier and are more severe than when the parathyroids alone are removed.

In many instances conjunctivitis and keratitis have been observed to follow the total extirpation of the thyroid gland.

Two other important symptoms observed after the latter operation remain to be mentioned; namely, a fall of the body temperature and anæmia. After a preliminary rise, the temperature gradually falls and becomes subnormal before death. Leucocytosis and diminution in the number of corpuscles are also observed.

When the thyroid gland is totally excised, and the animal survives the operation, it is extremely probable that one or more parathyroids have been left behind; but this cannot yet be asserted dogmatically. The effects of removal of the thyroid gland, leaving behind the parathyroids, have been studied in dogs. When the animal has recovered from the immediate effects of the operation it exhibits no signs of illness. In these cases a small portion of the thyroid has generally been left in addition to one or more parathyroids. Similar experiments have not yet been carried out in monkeys; but the effects of total extirpation of the thyroid gland in these animals have been carefully studied by Horsley, Munk, Edmunds, and others. Two classes of symptoms have been observed in them, the acute and the chronic. The acute symptoms closely resemble those observed in the dog. They appear within a few days after the operation. These symptoms have been summarised by Mr. Horsley as follows: "*Motion*, tremor, clonic spasm (paroxysmal), contracture, paresis, paralysis. *Sensation*, paræsthesia, then anæsthesia. *Reflexes* gradually diminished. Mental operations normal at first, are soon diminished in activity, and then follow apathy, lethargy, coma."

With these symptoms are associated subnormal temperature after an initial elevation, gradual anorexia after voracity, anæmia, leucocytosis, fall of blood-pressure, failure of nutrition with mucinous degeneration of the connective tissues, and usually atrophy and falling out of the hair. It is particularly interesting that "the eyelids become puffy with elastic œdema, the features grow heavy and coarse, the skin being rough in some cases, and the hair falling out." The duration of life averaged about twenty-four days. The chronic symptoms closely resembled those of myxœdema. They were observed in monkeys kept in a comparatively warm temperature.

The first few weeks after the operation were characterised by slight attacks of tremor and malaise. Then followed dulness of intellect, diminution of energy, and apathy alternating with idiotic activity. Persistent paresis and an attitude exactly resembling that of a human idiot or cretin were very interesting features. Although the animal fed voraciously it steadily emaciated. The hair fell out in quantity. The voice gradually altered until it became a hoarse croak. The scene was finally closed by coma.

In man the functions of the thyroid can be studied in the condition known as cachexia strumipriva, following on extirpation of the thyroid gland, and in myxœdema. The symptoms of cachexia strumipriva and those of myxœdema are identical and have elsewhere been fully described. It is not necessary to repeat what has been there said as to the removal of these symptoms by the internal administration of the thyroid gland, or of some preparation made from it. The logical conclusion is that the thyroid gland secretes some substance which is of great importance in the economy. The arrest of this internal secretion is followed by the changes in mind and body characteristic of myxœdema.

The statement has been made that in the fœtus, and during early infancy, the thyroid gland is relatively larger than in after-life; that its proportion to the weight of the body in the new-born infant is 1 to 240 or 400, at the end of three weeks it has become only 1 to 1160, and in the adult 1 to 1800. This statement was originally made by Huschke in 1844, but by a printer's error has been attributed to Krause in the various editions of Quain's *Anatomy*, including the last published in 1896. It is on the face of it extremely improbable that within three weeks of birth the thyroid should shrink to a third or even a fifth of its original weight. We have found the thyroid gland of infants a few days old to vary between fifteen and thirty grains, giving a proportion to body weight of 1 to 3000 or 1500. Dr. Stephen Mackenzie has published a series of observations on the weight of the thyroid body in persons dying from various causes. From these it would appear that there is no definite variation in the proportion between the weight of the thyroid gland and the body-weight in regard to age. Our own observations are perfectly in accordance with those of Mackenzie.

Attempts have been made to find the active principle of the thyroid gland. The substance which removes the symptoms of myxœdema is not destroyed by boiling nor by desiccation. Gland desiccated apparently preserves its properties unaltered for a long time if kept dry and not exposed to the air.

Mr. E. White has prepared a powder in the manner usually employed for the separation of ferments, and this has been found very efficacious in treatment. In the method employed the colloid substance is precipitated with calcium phosphate, and it is probably to the presence of this colloid that the properties of the powder are due.

Roos has shown that the active principle is not destroyed by boiling the gland in a 10 per cent solution of sulphuric acid. Baumann has endeavoured to obtain the principle from the precipitate which falls in this fluid on cooling. This precipitate is removed by filtration and treated with alcohol and petroleum-ether, to remove fat and fatty acids; it is then dissolved in a 1 per cent solution of caustic soda. This solution is filtered. The precipitate formed on adding dilute sulphuric acid is carefully washed and dried. A brown amorphous substance is obtained in this way which has been named "thyro-iodine," as it contains iodine in intimate chemical combination. It is almost insoluble in water, and is only slightly soluble in alcohol, although easily so in dilute alkalies.

The quantity of thyro-iodine present in the thyroid has been found to vary considerably. Only a slight trace of iodine has been found in abnormally large thyroids. There is less iodine in the glands of children than in those of adults.

The sheep's thyroid is relatively rich in thyro-iodine.

Thyro-iodine has been found experimentally to be as efficient as the thyroid gland itself in the treatment of myxœdema. This shows that it is a substance actually manufactured in the thyroid. In animals it is found that the amount of iodine present in the thyroid increases on administration of potassium iodide and other iodide-containing compounds; but the increase is most marked after the use of thyroid gland or thyro-iodine.

R. Hutchison has obtained the colloid matter of the thyroid separately, and has shown that it is therapeutically effective. He has found that the proteids of the gland are two in number. There is a nucleo-albumin present in small amount which is probably derived from the cells lining the vesicles. The other proteid is the colloid matter. This in addition to phosphorus contains a considerable amount of iodine. By gastric digestion the colloid can be split into two parts—a proteid part yielding albumoses and peptones, and an insoluble non-proteid residue which contains most of the iodine and all the phosphorus of the original colloid.

Besides the proteids there are also extractives, creatin, xanthin, as in other organs.

Neither the extractives nor nucleo-albumin have been found to produce any of the effects of thyroid substance when administered internally.

The colloid substance, as has been said, is therapeutically active. It is precipitated by adding acetic acid to a dilute alkaline extract of the fresh glands. It is purified by reprecipitation and by washing with alcohol and ether.

The proteid part of the colloid is much less active therapeutically than the non-proteid. This bears out Baumann's observation as to the importance of the iodine-containing compound, the so-called thyro-iodine.

W. M. Ord.
Hector Mackenzie.

Myxœdema

Definition.—A disease, closely related to cretinism, endemic and sporadic, if not identical with it; determined by the loss of function of the thyroid gland. The symptoms of myxœdema are also produced by complete operative removal of the thyroid gland.

The picture of the disease.—Thirty years ago the writer of this article had occasion to investigate the case of a lady suffering from myxœdema in a most definite form, and therefore offering complete opportunity of studying the symptoms and the relations of the disease. The patient, a lady of thirty-five, who had had several children, presented an appearance suggestive of Bright's disease; yet, although she was greatly swollen on the whole of her body, on careful examination the swelling did not appear to be due to an ordinary dropsy. There was nowhere any pitting on pressure, and there was no albuminuria in the slightest amount. The diagnosis of chronic Bright's disease without albuminuria at first suggested itself, but on further examination many symptoms not known to be related with Bright's disease came under the eye. The face, very much swollen in all parts, was particularly swollen in the eyelids, upper and lower, in the lips, and in the alæ nasi. There was a flush, very limited, over the malar bones, contrasting with a complete pallor over the orbital regions. The eyebrows were greatly raised by the effort to keep the lids apart. The skin of the face, and indeed of the whole body, was completely dry, rough and harsh to the touch; not exactly doughy, but giving a sensation of the loss of all elasticity or resilience. The hair was scanty, had no proper gloss, and was much broken. In the absence of all signs of visceral disease the condition of the nervous system was such as to attract much attention. The physiognomy was singularly placid at most times, less frequently heavy, with signs of somnolence; very rarely alert. In interviews the patient was imperturbably garrulous to a degree that could not fail to attract attention. For many minutes she would talk without cessation until obliged to stop and take a good breath. What she said was not altogether relevant, but it had to be said. All interrupting questions were disregarded. If, at the end of a small pause, she was asked to put out her tongue, she ignored the request, but at the end of a varying time, when her breath became short, she would put out her tongue for a long time. She dealt in the same way with questions put to her in respect of the points raised by her statements. Her letters were frequent, voluminous, and, as regarded handwriting, very good. Her speech was slow and laboured. There was some difficulty in it, evidently due to the swelling of the lips, but there was more than this: the words hung in a way that indicated nervous as well as physical difficulty, and inflexions of the voice were wanting. The tones of the voice were leathery, and suggested rather those of an automaton. The proper timbre was quite lost. Doubtless this was in part, again, due to obvious thickenings in the fauces and the larynx; but it did not in any way resemble the character of voice observed in ordinary swellings of those parts. Her temper was singularly equable, she was the most tender and solicitous of mothers, and in a long course of years during which she was under the writer's observation no word of unkindness or suspicion fell from her lips. Lethargy was an impressive part of her mental condition. Memory was slow, but correct. She thought slowly, performed all movements slowly, and was slow in receiving impressions. Her toilet, and she was no fashionable person, occupied hours. Her household duties could never be overtaken, and she had to seek assistance. Her gait presented a distinct ataxic quality. As her bulky body moved across a room there occurred at each step forward a quiver running from the legs upwards, such as may be seen in people under the influence of great emotion, as in a Lady Macbeth. This appeared to be due to a want of complete concert in the action of the flexors and extensors of the body, the flexors acting for the most part in advance. The interval between the action of the two sets of muscles was at some times extreme enough to determine falls, not in any way produced by obstacles. She fell forwards on her knees, and, as a result, she sustained fracture of the patella on one side, and of the patellar tendon on the other. Similar conditions existing in the head and neck produced excessive distress. From time to time the head would fall forward in spite of all voluntary effort to prevent it. The chin would then rest on the upper part of the sternum, as is seen in cretins. Sometimes by prolonged exertion of the will, sometimes with the assistance of the hands, the head would be raised, not always to good effect; for unless great care were exercised the head would fall backwards with a suddenness that was alarming. There was no obvious defect of the sense of touch, but it must be admitted that the speed of the reception of tactile sensations was not noted. After the establishment of the disease she bore two children; on both occasions severe post-partum hæmorrhage occurred. She had no other hæmorrhages. The first impression was, as I said above, that the case was one of Bright's disease without albuminuria. The urine was examined regularly for years without detection of albumin, and there were no such changes in the heart and arteries as belong to Bright's disease. After ten years, however, albumin appeared in the urine, and the patient died ultimately with symptoms of contracting granular kidney. A post-mortem examination could not be obtained, and therefore the condition of the thyroid gland and of the kidneys cannot be recorded.

Symptoms.—I will now proceed to state in detail the development of our knowledge of this disease. In 1875 Sir William Gull contributed to the Clinical Society a paper on "A Cretinoid State supervening in Adult Life in Women," in which he graphically described the symptoms, but did not discuss the pathology. In 1878 the writer read before the same Society a paper in which he ventured to give the name myxœdema to the disease, after describing the symptoms and discussing the pathology so far as it could be determined by autopsies of patients for some years under his care, and by examination, chemical and microscopical, of the various tissues. To these early observations many have been subsequently added. The general results of the whole series of observations may now be stated. In the first place, it appears that myxœdema affects men also, though in a much smaller proportion than women; men apparently contribute about 10 per cent of all the cases. Both in women and in men there is a remarkable agreement in the main symptoms, when the disease is complete. The whole body is swollen and unwieldy, the swelling being partly produced by an enormous thickening of the skin, partly by the presence of a soft fat. The skin, besides being swollen, is excessively dry, perspiration being very rarely observed. On the trunk and limbs in particular the skin becomes rough and scaly, almost as if it were sanded. The swelling is not quite equally distributed, but is modified by the relations of the skin in the various parts of the body. Thus, large soft swellings are observed in the supraclavicular region, and the hands and feet become greatly enlarged and flattened; the condition of the hands has been aptly described as spade-like by Sir Wm. Gull. They are usually very broad, the fingers are much flattened, and the hand loses most of the expression related with the actions of life. The most noteworthy external changes are those which are seen in the face. With a great general swelling it is to be noted that certain of the features are particularly altered. The eyelids, upper and lower, are excessively thickened and hang in translucent folds. So also both lips are usually greatly swollen, and the alæ nasi are greatly broadened. The skin of the face is pallid, excepting over the malar bones, where a pink flush, abruptly limited by the lower margin of the orbit, is usually present. There is no pitting of the skin on the face or elsewhere; it presents everywhere the same sort of doughy consistence described on a previous page. As in cases of ordinary dropsy, involving the face, the victims come to resemble one another very much, so it is in myxœdema; but not quite in the same way, for the lines of expression, while altered, are not obliterated as in simple œdema. The general expression is one of heaviness and dulness. The eyebrows are generally very much raised and arched by the effort necessary to keep the lids apart. There is great diminution in the mobility of the features, particularly of the mouth; the eyelids often take an oblique direction, such as is seen in Mongolian tribes. The general alteration of physiognomy is intensified by the state of the hair, which first loses its natural gloss, becomes fragile, rough, and scanty, often almost to baldness. The swollen ears then stand out with marked prominence. Moles are often developed, especially on the trunk.

The same swelling which is seen in the skin affects the mucous membranes. The inside of the lips and cheeks is tumid, and is very apt to be bitten during mastication. The soft palate is generally found swollen to translucency and with great decrease of mobility. The teeth, like the hair, undergo degeneration, become loose in their sockets, or fall out. The speech is altered in so uniform a way that a diagnosis may almost be made when a patient, unseen, is heard talking. The words come very slowly and deliberately, the voice is monotonous and of a leathery timbre, no doubt much determined by the swelling of the throat, and is evidently produced with considerable effort owing to the swelling of the lips. This can be well recognised if the patient be watched as he speaks, the words seeming to be squeezed out of the lips with much difficulty. As already mentioned, there is probably a nervous as well as a mechanical cause for this change in speech. The gait already described is typical of myxœdema, and the tendency to fall, as mentioned in the first case, usually exists, to the production of many accidents. The movements of the hands are also limited and awkward, partly by reason of the swelling, partly by the slow sensation. "All the fingers are thumbs," as a patient once remarked. Thought and movement are slow, and there is a slowness in the reception of tactile sensations, constituting a marked bradæsthesia. There is considerable variation in the mental condition; most of the patients are persistently and obstinately garrulous, but all have not the placid temper noted in the first case.

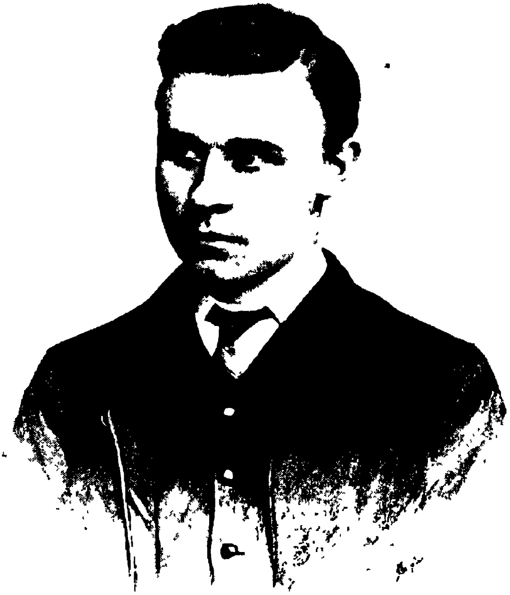

FIG. 7.—Before myxœdema

There is generally a tendency to a mixture of irritability with the torpor, and a proneness to unfounded suspicions of many kinds. If not suspicious of others, patients will come to be suspicious of themselves. This condition may be developed to the point of insanity, and will often survive other symptoms of the disease when the general illness appears to have yielded to treatment. Such patients have to be watched very carefully, as at times they are tempted to suicide; many of them are to be found in the wards of asylums. The temperature of the body is generally below the normal, 97° or 96° Fahrenheit being a common record; and the patients are extremely sensitive to cold. Where the temperature ranges at all above the normal it must be recognised at once as pyrexial. The urine is generally reduced in quantity without much change in its specific gravity. As a rule it contains no albumin or sugar, but the daily excretion of urea is diminished, even under ordinary diet. The catamenia are usually regular, but apt to be excessive. Pregnancy may occur after the full establishment of the disease, and, as already noted, hæmorrhage is to be dreaded. In connection with pregnancy fluctuations in the swelling of the body often occur. There is sometimes an increase, more commonly a decrease, so that in early stages the patient may resume almost a natural appearance during pregnancy. Independent of pregnancy, moreover, the amount of swelling is apt to vary. There is usually a first period in which the swelling affects some parts more than others, and disappears and recurs in one part or another somewhat rapidly. Then comes the establishment of the definite disease. Finally, in later stages, particularly where some additional ailment is intruded, the skin becomes flaccid and dull, though without resumption of its natural function. In addition to the tendency to uterine hæmorrhage bleeding is very common in myxœdema. It will often follow the extraction of a tooth so loose as to seem ready to drop away from the gum, and may be very intractable for hours or days. Bleeding from the nose is also common, and small wounds give much trouble in this respect.

Pathology.—There can be no doubt that Sir William Gull struck the key-note of the etiology of this disease when he used the word "cretinoid." It is now generally recognised that absence of the function of the thyroid gland is the essential cause of myxœdema. In a great majority of cases the gland is atrophied and its proper structure lost. In such cases the wasting of the gland can mostly be recognised during life, very often it may not be felt at all. But in certain cases the gland may be actually enlarged, either by destructive infiltration, by new growth, or by the presence of excess of fibrous tissue. The fact that myxœdema is chiefly a disease of women suggests a relation of the destruction of the thyroid with changes in the structure of the gland related with menstruation or pregnancy. It is to be noted that the disease occurs more often in married than in single women; and it must be remembered that it is chiefly in women an affection of adult and middle life, in marked contrast to the appearance in earlier life of exophthalmic goitre. There can be no doubt of the frequent existence of an active congestion, bordering on an inflammatory condition, occurring in the thyroid gland at the time of menstruation. Such changes are distinctly marked in exophthalmic goitre. It appears to me that probably the atrophy of the gland, productive of myxœdema, is frequently due to inflammatory destruction of the gland tissue. Several cases have now been recorded in which the symptoms of exophthalmic goitre have been followed and replaced by those of myxœdema, the once greatly enlarged thyroid having become much diminished, or been reduced to a very small size. Here the sequence of atrophy upon a destructive inflammatory enlargement is strongly indicated. It has occurred to me to watch several such cases undergoing this transition, and to note that myxœdematous swelling has appeared before the general symptoms of exophthalmic goitre have passed away.

Originally the idea that the thyroid played a part in myxœdema was partly based on the observations of Curling and others in regard to sporadic cretinism, in which the great diminution or absence of the thyroid had been well established. It is now well known, originally through the observations of Kocher and Reverdin, that complete removal of the thyroid body in cases of goitre is followed by symptoms indistinguishable from those of myxœdema. Operations consisting in the removal of the thyroid of animals, particularly of monkeys, and more especially the experiments of Horsley, have shown that symptoms resembling those of myxœdema can be so produced.

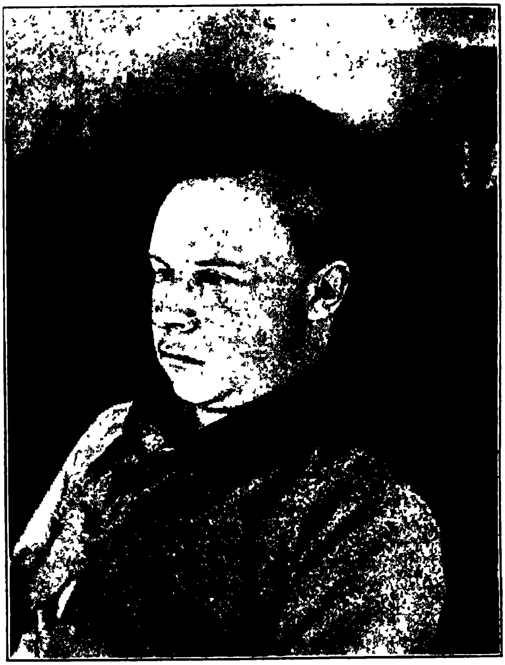

Fig. 8.—Pronounced myxœdema.

Morbid anatomy.—Apart from the change in the thyroid, the tissues in the body, when observed in cases of full development of the disease, present some remarkable appearances. Throughout the body the connective tissue is swollen in some such way as is suggested by the state of the skin. When the skin is cut into, there is no escape of serous fluid from it, and it remains unshrunken as though soaked in jelly. In microscopic sections it can be recognised that the connective tissue is interpenetrated by an almost transparent or faintly granular material, separating the fibrils, increasing greatly the bulk of the connective tissue in all parts, and determining compression of glandular structures. In the skin, for example, the hair-bulbs and sweat-glands undergo great compression, which is no doubt the explanation of the impaired nutrition and falling out of the hairs. Similar changes can be observed in the viscera: in the liver, for instance, the cells can be seen separated from one another, and evidently compressed. In some cases the kidneys have been found much enlarged and much toughened, showing, microscopically, the presence of large quantities of this intrusive substance strangling the secreting structures. In my first investigations it appeared to me that this substance was a mucin-yielding modification or infiltration of the connective tissue. This view has not altogether been accepted, although in Mr. Horsley's experiments mucin was found in the skin of monkeys previously operated upon. Seeing that a large number of the victims of myxœdema undergo great shrinking or emaciation before death, it is very probable that the infiltrating material will, in such cases, have undergone considerable absorption; and the fact that mucin has not been found in such cases is hardly an argument against its presence during the full development of the disease.

Prognosis.—Untreated myxœdema is usually progressive in its character, though it may last for many years, the patients either becoming wasted, and dying of inanition, passing into coma, or dying with signs of bulbar affection. In a few cases death has been the result of cerebral hæmorrhage. In a certain proportion, intercurrent disease, either of an acute kind, or notably tubercular affections, may lead to death. It has been seen that symptoms like those of contracting granular kidney may be observed and may prove fatal.

The prognosis in cases of untreated myxœdema, particularly in the poor and ill-clad, is most unfavourable. In cases of fairly early or fully-developed myxœdema the results of treatment by thyroid justify a strong expectation of cure; but in cases of long duration, where the age is for the most part advanced and shrinking has set in, less confidence can be entertained. In such cases, although the swelling may be further diminished, the patient will often sink into fatal weakness, in spite of the use of the thyroid backed up by tonics. More has yet to be learned of cases in which much mental disorder exists. It is to be feared that the prognosis here also is unfavourable.

Treatment.—The early treatment of myxœdema consisted in giving tonics, such as iron, arsenic, and the hypophosphites; in giving diaphoretic drugs, such as jaborandi; and in applying baths. Great care was found to be necessary in the protection of patients from cold. Sufferers from myxœdema have all their symptoms aggravated and suffer from great weakness and depression when exposed to cold; though it is a singular fact that they are often not conscious of any discomfort from impact of cold air, this being doubtless due to the thickened and insensitive condition of the skin. Where patients were able to afford it they were sent away during the winter and spring to warmer climates than our own. Of late years a most complete and successful revolution has occurred in the treatment of myxœdema. The evolution of this treatment has been gradual. At first an endeavour was made to replace the lost thyroid by the introduction of the thyroid glands of animals, or portions of bronchoceles within the tissues or cavities of the human body. It was found that while some temporary relief was afforded, these introduced substitutes in a short time underwent absorption, and ceased to be effective. Later it occurred to Dr. George Murray of Newcastle to practise regular hypodermic injections of a carefully-prepared glycerine extract of the thyroid gland of the sheep. The injections used represented individually only a fraction of a thyroid gland, but, being repeated at regular intervals, were found to bring about a rapid melting away of the swelling and removal of the attendant symptoms. Dr. Hector Mackenzie subsequently tried with great success the internal administration of the thyroid gland of the sheep. It appears that, taken internally, either in a raw state or in the form of various extracts and dry preparations, the drug is one of great curative power. In fact it is quite possible to give too large doses of it with very unpleasant and injurious effects. The immediate effect of the administration of the extract of the thyroid gland to a patient suffering from the characteristic symptoms of myxœdema is to raise the temperature of the body rather quickly to the normal. In fact, too large and too frequent doses will produce violent pains and some pyrexia. Then follows a diminution, generally gradual, sometimes very

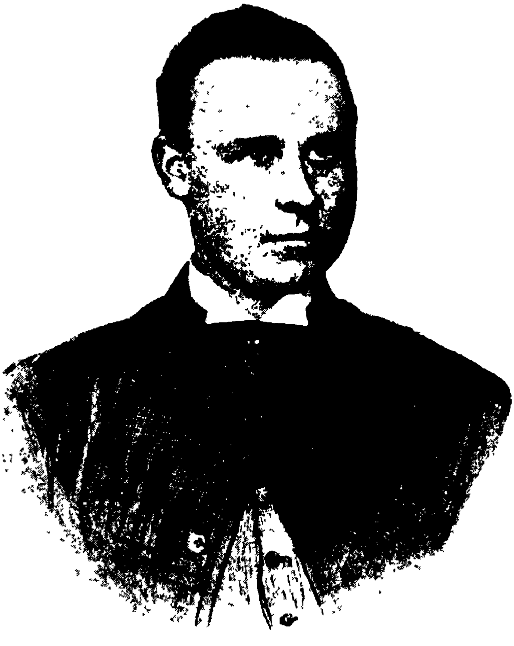

FIG. 9.—The same patient as in Figs. 7 and 8 after two years of treatment by administration of preparation of thyroid gland

speedy, of the bulk of the body, with restoration of the functions of the skin, and, for the most part, a restoration also of the natural conditions of the nervous system. Sometimes, however, where marked symptoms of mental disorder have been present, they are abated only after long treatment; and it must be admitted that in a few cases they seem actually to be aggravated. In the earlier days of the administration of thyroid, the quantity of the urine, and the total excretion of nitrogen, particularly in the form of urea, are increased. As time goes on, the frequency of administration or the dose may be diminished, but discontinuance of administration for any long period is followed by return of symptoms. Apparently it is necessary to maintain the treatment throughout life or at least for many years. Experience shows that, even while reaping so great a benefit from the use of the thyroid, we are still bound to shield our patients as far as possible from exposure to cold.

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REFERENCES

1. Abercrombie, J. "A Case of Myxœdema in a Young Subject," *Tr. Clin. Soc. Lond.* 1890, xxiii. 240.—2. Abrahams, R. "Myxœdema treated with Thyroid Extract; Report and Presentation of a case," *Med. Record*, N.Y. 1895, xlvii. 429-431.—3. Adams, J. "Two Cases of Myxœdema treated by Thyroid Feeding," *Glasgow Med Journ.* 1893, xl. 196-198.—4. Alexander, J. W. "Note on a Case of Myxœdema occurring in an Insane Patient," *Med. Chron.* Manchester, 1893, xviii. 175-178.—5. Anderson, J. A. "Ett fall af myxodem behandladt mid thyreoideatabletter [Case of . . . treated with thyroid tablets]," *Hygiea*, Stockholm, 1896, lviii. 303-326.—6. Anderson, T. McC. "The Treatment of Myxœdema," *Practitioner*, Lond. 1893, l. 36-44.—7. Anderson, W. "Patient with Congenital Myxœdema shown after Treatment with Thyroid Extract," *Glasgow Med. Journ.* 1895, xliii. 291-293.—8. Anderson, W. M. A. "A Case of Myxœdema in the Adult, following Bronchocele in the Child; successfully treated by Hypodermic Injections of Thyroid Juice and by Feeding with Thyroid Glands of the Calf; with Notes on the Treatment of Obesity and Chlorosis," *Journ. Laryngol.* Lond. 1893, vii. 68-70.—9. Anson, G. E. "Treatment of Myxœdema by Thyroid Juice," *N. Zealand Med. Journ.* Dunedin, 1893, vi. 169-176.—10. Arnozan, X. "Un cas de myxœdème guéri par la médication thyroidienne," *Journ. de méd. de Bordeaux*, 1894, xxiv. 397.—11. *Idem.* "Un cas de myxœdème," *Mem. et bull. soc. de méd. et de chir. de Bordeaux* (1894), 1895, 466-472.—12. Ayres, S. "A Case of Myxœdema treated by Sheep's Thyroid," *Journ. Nerv. and Mental Dis.* N.Y. 1894, xxi. 481-85.—13. Baber, E. C. "Feeding with fresh Thyroid Glands in Myxœdema," *Brit. Med. Journ.* 1893, i. 10.—14. *Idem.* "Traitement du myxœdème par alimentation avec la glande thyroide fraiche," *Revue internat. de rhinol. otol. et laryngol.* 1894, iv. 25.—15. Balzer, F. "Myxœdème; traitement par l'injection du corps thyroide frais," *Ann. de dermat. et syph.* Paris, 1895, 3 sér. vi. 378; *Bull. soc. franç. de dermat. et syph.* Paris, 1895, vi. 169.—16. Barton, J. H. "Case of Myxœdema treated by Injection of Sheep's Thyroid at Mentone," *Dublin Journ. Med. Sci.* 1893, xcv. 431-433.—17. Barron, A. "Two Cases of Myxœdema treated by Thyroid Injections," *Brit. Med. Journ.* Lond. 1892, ii. 1384.—18. Barrow, A. "On Myxœdema," *Liverpool M.-Chir. J.* 1893, xiii. 135-149.—19. Beadles, C. F. "A Case of Myxœdema with Insanity treated by the Subcutaneous Injection of Thyroid Extract," *Brit. Med. Journ.* 1892, ii. 1386.—20. *Idem.* "The Thyroid Treatment of Myxœdema associated with Insanity," *Lancet*, 1894, i. 400.—21. Beatty, W. "A Case of Myxœdema successfully treated by Massage and Hypodermic Injections of the Thyroid Gland of a Sheep," *Brit. Med. Journ.* London, 1892, i. 544.—22. *Idem.* "A Case of Myxœdema successfully treated by Injections of Extract of Sheep's Thyroid," *Trans. Royal Acad. Med. Ireland*, 1892-93, xi. 87-92.—23. *Idem.* "A Case of Myxœdema successfully treated by Injection of Extract of Sheep's Thyroid," *Dublin Journ. Med. Sci.* 1893, xcv. 375-379.—24. Beccaria, F. "Osservazioni oftal-

mometriche in una malata affetta da mixoedema, per effetto di compressione diretta sul cervello," *Gior. d. r. Accad. di med. di Torino*, 1891, 3 s. xxxix. 89-96.—25. *Idem.* "Osservazione oftalmometriche in una malata affetta da mixoedema, per effetto di compressione diretta sul cervello," *Ann. di ottal.* Pavia, 1891-2, xx. 96-103.—26. De Becker. "Traitement d'un cas grave de myxœdème par ingestion de glandes thyroides du mouton ; guérison," *Presse méd. Belg.* Brux. 1894, xlvi. 225.—27. Bell, R. E. "A Case of Myxœdema," *Boston Med. and Surg. Journ.* 1894, cxxx. 364.—28. Benson, J. H. "Case of Myxœdema of long standing treated by Administration of Thyroid Extract by Mouth," *Brit. Med. Journ.* 1893, i. 795.—29. De Boeck. "Un cas de myxœdème avec troubles psychiques traité par les injections de suc thyroidien," *Journ. de méd.-chir. et pharmacol.* Brux. 1892, xciv. 484-488.—30. Bohncke, Carl A. B. *Zur Myxodemfrage*, Berl. 1890 ; O. Francke.—31. Bouchard. "Deux cas de myxœdème traités par les injections de suc thyroidien," *Bull. méd.* Par. 1892, vi. 1263.—32. Bourneville. "Nouveau cas d'idiotie avec cachexie pachydermique (myxœdème infantile), avant le traitement par l'injection stomacale de glande thyroide," *Compt. rend. soc. de biol.* Par. 1896, 10 s. [illegible]ii. 467.—33. *Idem.* "Nouveau cas d'idiotie avec cachexia pachydermique (myxœdème infantile) ; après le traitement," *Compt. rend. soc. de biol.* Par 1896, 10 s. iii. 698-701.—34. *Idem.* "Trois cas d'idiotie myxœdémateuse traités par l'ingestion thyroidienne," *Archives de neurol.* Paris, 1896, 2 sér. 1-28.—35. *Idem.* "Cinq cas d'idiotie myxœdémateuse traitement par l'ingestion de glande thyroide," *Bull. et mém. soc. méd. des hôp. de Paris*, 3 sér. xiii. 1895, 32-39.—36. *Idem.* "Cas de myxœdème congénital," *Progrès méd.* Paris, 1895, 3 sér. ii. 33, 49.—37. Boyce, R., and C. F. Beadles. "Enlargement of the Hypophysis Cerebri in Myxœdema ; with Remarks upon the Hypertrophy of the Hypophysis ; associated with Changes in the Thyroid Body," *Jour. Path. and Bacteriol.* Edinb. and Lond. 1892, i. 223-239, 2 pl.—38. Bradley, O. C. "Myxœdema in the Horse," *Vet. Jour. and Ann. Comp. Path.* Lond. 1893, xxxvi. 309-311.—39. Bramwell, B. "Myxœdema," *Atlas of Clin. Med.* Edinb. 1891, ii. pt. l. 1-16, 3 pl.—40. *Idem.* "The Clinical Features of Myxœdema," *Edinb. Med. Journ.* 1892-3, xxxviii. 985-995.—41. *Idem.* "The Thyroid Treatment of Myxœdema and Sporadic Cretinism, with Notes of Twenty-three Cases of Myxœdema and Five Cases of Sporadic Cretinism treated by Thyroid Extract," *Edinb. Hosp. Rep.* 1895, iii. 116-249.—42. Brissaud and Souques. "Un cas de myxœdème opératoire traité par l'ingestion de glande thyroide de mouton," *Cong. de méd. aliénistes et neurol. de France* . . . [Proc. verb etc.], 1894, Paris, 1895, v. 518.—43. *Idem.* "Un cas de myxœdème congénital traité et guéri par l'ingestion de corps thyroide de mouton," *Bull. et mém. soc. méd. des hôp. de Paris*, 1894, 3 sér. xi. 236-41, 1 plate.—44. Brown, Ethel D. "Case of Myxœdema, three and a half Months' Treatment with Thyroid Glands," *Med Rec.* N.Y. 1893, xliv. 142.—45. Buchanan, R. M. "A Case of Myxœdema with Microscopic Examination of the Thyroid Gland," *Glasgow Med. Journ.* 1892, xxxviii. 329-333.—46. *Idem.* "Case of Myxœdema in an Early Stage," *Glasgow Med. Journ.* 1893, xxxix. 440-442.—47. *Idem.* "Case of Myxœdema, with Microscopic Examination of Thyroid Gland," *Jour. Glasg. Path. and Clin. Soc.* 1891-3, iv. 150-155.—48. Burckhardt, O. "Cas de myxœdème guéri par le thyroidine ; mort par broncho-pneumonie ; absence totale de corps thyroide," *Revue méd. de la Suisse romande*, Genève, 1895, xv. 341-346.—49. Zum Busch, J. P. "Die Schilddrusenbehandlung bei Myxodeme und verschiedenen," *Hautkrankheiten dermat. Zeitschr.* Berl. 1894-95, ii. 433-459.—50. Buys, E. "Contribution à l'étude du principe anti-myxœdémateux de la glande thyroide," *Revue Internat. de rhinol. otol. et laryngol.* Paris, 1895, v. 85.—51. Buzdygan, M. "*Myxoedema Pryegl. lek.* Krakow, 1891, xxx. 52, 65, 82, 95.—52. *Idem.* "Zwei Falle von Myxodem," *Wien. klin. Wochenschr.* 1891, iv. 570-573.—53. Calvert, J. "A Case of Myxœdema treated by the fried Thyroids of Sheep," *Trans. Clin. Soc. Lond.* 1892-3, xxvi. 237.—54. Campbell, W. M. "Case of Myxœdema with Glycosuria treated with Thyroid Extract," *Liverpool Med.-Chir. Journ.* 1894, xiv. 452-454.—55. Cauter, C. "Myxœdème et goitre exophtalmique," *Ann. soc. méd.-chir. de Liège*, 1894, xxxiii. 12-25.—56. Chopinet. "Myxœdème ou cachexie pachydermique observée chez une jeune fille de vingt-trois ans ; guérison presque complète au moyen des injections sous-cutanées d'extrait liquide du corps thyroide de mouton," *Compt. rend. soc. de biol.* Par. 1892, 9 s. iv. 602-607.—57. Clark, A. C. "Case of Myxœdema with Tumours of the Brain," *Edinb. Med. Journ.* 1890-1, xxxvi. 1012-1016.—58. Clouston, T. S. "The Mental Symptoms of Myxœdema and the Effect on them of the Thyroid Treatment," *Journ. Mental Science*, xl. 1894, 1[illegible]11.—59. Cocking, W. T. "Notes of a Case of Myxœdema treated by Thyroid Feeding," *Sheffield Med. Journ.* 1892-3, i. 312-314, 1 pl.—60. Comby, J. "Myxœdème chez une fillette de deux ans et demi; traitement par de régime thyroidien; amélioration," *Méd. inf.* Paris, 1894, i. 578-80.—61. CONSOT. "Idiotie avec cachexie pachydermique (idiotie myxœdémateuse)," *Bull. soc. de méd. ment. de Belg.* Gand et Leipzig, 1891, 421-427, 2 phot.—62. CORKHILL, J. G. G. "Myxœdema, with enlarged Thyroid, treated by Subcutaneous Injections of Thyroid Extract; recovery," *Brit. Med. Journ.* 1893, i. 8.—63. COWLES, W. N. "A Case of Myxœdema treated by Thyroid Extract," *Boston Med. and Surg. Journ.* 1894, cxxx. 167.—64. CRARY, G. W. "Myxœdema, acquired and congenital, and the Use of the Thyroid Extract," *Amer. Journ. Med. Science*, 1894, n.s. cvii. 515-531.—65. *Idem.* "A Case of Myxœdema, treated with Thyroid Extract by the Stomach, and a Description of the Method of preparing the Extract," *Med. Rec.* N.Y. 1893, xliii. 739-743.—66. CURTIS, H. H. "The Throat Appearances in Myxœdema," *Journ. Amer. Med. Asso.* Chicago, 1894, xxiii. 486.—67. DANDOIS. "Un cas de myxœdème infantile," *Revue méd.* Louvain, 1894-95, xiii. 49-55.—68. DAVIES, A. T. "A Case of Myxœdema," *Trans. Clin. Soc. Lond.* 1891-92, xxv. 285.—69. *Idem.* "A Case of Myxœdema in a Male successfully treated by Injections of Sheep's Thyroid Juice," *ibid.* 306, 1 b. 1 pl.—70. *Idem.* "A Case of Myxœdema," *ibid.* 306.—71. *Idem.* "A Case of Myxœdema in a Male treated by dried Thyroid Extract given by the Mouth," *Tr. Clin. Soc. Lond.* 1891-93, xxvi. 234-236.—72. *Idem.* "Myxœdema and its recent Advances in its Therapeutic Treatment," *Internat. Clin.* Phila. 1893, 3rd s. ii. 74-83.—73. *Idem.* "A Clinical Review of the Treatment of Myxœdema and its bearing on certain other Diseases," *Internat. Clinics*, 1893, 3rd ser. iii. 12-21.—74. DEBOVE. "Myxœdème," *Ann. de méd. scient. et prat.* Par. 1894, iv. 201.—75. DESSAU, S. H. "Lipomatosis Universalis, with Symptoms of obscure Nerve Lesions, versus Myxœdema," *Clin. Recorder*, N.Y. 1896, i. 15.—76. DUCKWORTH, Sir D. "Sequel to a Case of Myxœdema reported to the Society, November 1880," *Tr. Clin. Soc. Lond.* 1891-92, xxv. 224-226.—77. DUKE, E. "Myxœdema," *Birming. M. Rev.* 1893, xxxiv. 86-89.—78. DUNLOP, G. H. M. "Six Cases of Myxœdema treated by Thyroid Feeding," *Edinb. M. J.* 1892-93, xxxviii. 1005-1014.—79. DRYSON, W. "A Case of Myxœdema," *Sheffield M. J.* 1892-93, i. 30-35, 1 pl.—80. ELAM, G. "A Case of Myxœdema treated with Thyroid Extract," *Lancet*, 1893, ii. 631.—81. ELDER, N. "A Case of Myxœdema treated with Thyroid Extract," *Brit. Med. Journ.* 1895, i. 697.—82. EMBLEY, E. H. "A Case of Myxœdema with Symptoms simulating Ovarian Tumour," *Austral. Med. Journ.* Melbourne, 1895, New Ser. xvi. 277-280.—83. D'EVELYN, F. W. "Myxœdema," *Pacific M. J.* San Fran. 1893, xxxvi. 469-476.—84. EWALD, C. A. *Die Erkrankungen der Schilddrüse, Myxodem und Cretinismus*, Wien, 1896, A. Holder, 253 pp., 1 map.—85. *Idem.* "Ueber einen durch die Schilddrusen Therapie gehalten Fall von Myxodem nebst Erfahrungen über onderweitige Anwendung von Thyreoideapraparaten," *Verhandl. d. Ber. med. Gesellsch.* (1894), 1895, xxv. pt. 2, 284-306 [Discussion], pt. 1, 179.—86. FENWICK, H. "Myxœdema treated by Injections of fresh Thyroid Juice," *Lancet*, Lond. 1892, 11, 941.—87. FERRIER, D. "Notes of a Case of Myxœdema treated by Thyroid Extract (complete recovery)," *Clin. Sketches*, 1895, i. 36-38, illustrations.—88. FEULARD, H. "Cas de myxœdème congénital chez un sujet féminin âgé de 19 ans et demi," *Bull. soc. franç. de dermat. et syph.* Par. 1890, i. 232-237.—89. FINLAY, D. W. "On a Case of Myxœdema," *Internat. Clin.* Philad. 1892, 2nd s. ii. 1-7, 1 pl. 1 diagram.—90. FOX, E. L. "A Case of Myxœdema treated by taking Extract of the Thyroid by the Mouth," *Brit. Med. Journ.* 1892, 11, 941.—91 FRASER, C. "The Treatment of Myxœdema with Thyroid Gland," *Atti d. xi. Congr. Med. Internaz. Roma*, 1894, iii. Farmacol. 117.—92. GODART-DANHIEUX. "Un cas de myxœdème avec ascite traité par l'extrait thyroidien," *Journ. de méd.-chir. et pharmacol.* Brux. 1895, 433-441.—93. *Idem.* "Un cas de myxœdème," *ibid.* 643-645.—94. GORDINIER, H. C. "Report of Two Cases of Myxœdema, with One Autopsy," *N. York Med. Journ.* 1892, lvi. 169-172.—95. GOWAN, B. C. "Myxœdema and its Relation to Graves' Disease," *Lancet*, 1895, i. 478-580.—96. HAIG, A. "The Effect of Thyroid Extract in Myxœdema complicated by Angina Pectoris," *Lancet*, 1895, ii. 873.—97. HALBERT, H. V. "Myxœdema illustrated by a Case: Clinique," *Chicago*, 1895, xvi. 385-394.—98. HALE, G. E. "Four Cases of Myxœdema treated by Injections of Thyroid Extract," *Brit. Med. Journ.* 1892, ii. 1428.—99. HAROLD, J. "Cases of Myxœdema treated by Thyroid Gland," *Practitioner*, Lond. 1894, liii. 100-105.—100. *Idem.* "A Case of Myxœdema treated by Thyroid Gland," *Lancet*, 1894, ii. 434-436.—101. HARVIS, T., and G. A. WRIGHT. "Myxœdema treated by Thyroid Grafting," *Lancet*, 1892, i. 81-84.—102. HAYES, W. A. "Case of Myxœdema," *Bristol Med.-Chir. Journ.* 1894, xii. 230-232.—103. HENRY, J. P. "A Case of Myxœdema cured by Thyroid Extract," *Brit.*

Med. Journ. 1893, i. 737.—104 Hodge, G. "Myxœdema," *Am. Med.-Surg. Bull.* N.Y 1896, ix. 724.—105. Holman, C. "A Case of Myxœdema treated by Thyroid Feeding," *Brit. Med. Journ.* 1893, i. 114.—106. Hopman. "Operatives Myxodem schwerer Art von ungewohnlich langer Dauer," *Deutsche med. Wochenschr.* 1893, xix. 1357.—107. Houel, E. "Note sur une malade présentant un état général cachectique particulier (myxœdème), améliorée par des injections d'extrait de corps thyroide," *N Montpel. méd.* 1895, iv. 271-282.—108. Hun, H. "The Treatment of Myxœdema by Feeding with the Thyroid Gland," *Albany M. Ann.* 1894, xv. 1-17.—109. Immerwol, V. "Du myxœdème infantile," *Méd. inf.* Paris, 1894, i. 558-66.—110. Immerwolt. "Mittheilung uber einen Fall von kindlichem Myxoedem (sporadic cretinism) mit abweichenden hystologischem Befund der Haut," *Atti d. xi. Congr. Med. Internaz. Roma*, 1894, iii. Pediat. 141-143.—111. Janicke, O. "Ueber Myxoedem mit Demonstration eines einschlagigen Falles," *Jahresb. d. schles. Gesellsch. f. vaterl. Kult.* 1890, Bresl. 1891, lxviii. med. Abth. 19.—112. Jaunin, P. "Observation d'un nain myxœdémateux traité par les préparations thyroidiennes," *Revue méd. de la Suisse romande*, Genève, 1896, xvi 34-38.—113. Kasche, Heinrich. *Kachexia thyreopriva und Myxodem*, Berl. 1893, G. Schade. 44 pp.—114. Kenny, F. H. "A Case of Myxœdema," *Australian Med. Journ.* 1893, n.s. xv. 634-641.—115. Kimball, R. B. "A Case of Myxœdema with unusual Features and rapid Recovery," *Med. Record*, N.Y 1893, xliv. 814.—116 Kinnicutt, F. P. "Myxœdema; the Functions of the Thyroid Gland and the present Method of Treatment of Myxœdema," *Tr. Assoc. Amer. Physicians*, Philad. 1893, viii, 309-332.—117. *Idem.* "Myxœdema; the Functions of the Thyroid Gland, and the present Method of Treatment of Myxœdema," *Med. Rec* N.Y. 1893, xliv. 449-455.—118. Kirk, R. "Notes on Cases of Myxœdema," *Lancet*, Lond. 1893, ii. 743-745.—119. Klee, F. E. "Et. Tilfaelde af Myxoedem; Restitution rea smaa doser Thyreoidin i et laengere Tidsrum," *Ugesk f. Laeger*, Kjobenh. 1896, 5 R. iii. 145-151.—120. Kohler, R. "Myxodem, auf Syphilis berahend," *Berl. klin. Wochnschr.* 1892, xxix. 743.—121. *Idem* "Myxodem auf seltener Basis," *Berliner klinische Wochenschr.* 1894, xxxi. 927.—122. Kraepelin, E "Ueber Myxodem," *Deutsches Arch. f. klin. Med.* Leipz. 1891-92, xlix. 587-603.—123. Krauss, W. C. "Observations on a Case of Myxœdema," *Journ. Nerv. and Ment. Dis.* N Y. 1893, xx. 685-688.—124. Krówczyúski, Z. "Myxœdema," *Medycyna*, Warszawa, 1892, xx 129-132—125. Laache, S. "Ueber Myxodem und dessen Behandlung mit innerlich dargereichter Glandula thyreoidea," *Deutsche med. Wochenschr.* Leipz. u. Berl. 1893, xix. 257-259.—126. Leichtenstern, O. "Ein mittels Schilddrusenmjection und Futterung erfolgreich behandelter Fall von Myxoedema operativum," *Deutsche med. Wochenschr.* 1893, xix. 1297, 1333, 1354.—127. *Idem.* "Zur Geschichte der Myxodemfrage," *Deutsche med. Wochenschr.* 1894, xx. 251.—128. Leszynsky, W. M. "A Case of Sporadic Myxœdematous Cretinism," *Post-Graduate*, New York, 1894, ix. 413-415.—129. Little, J. "Sequel of a Case of Myxœdema treated by Thyroid Juice," *Dublin Journ. Med. Sci.* 1894, xcvii. 293-295.—130. Loewy, A. "Ein Fall von Myxodem bei cretinartigem Zwergwuchs," *Berl. klin. Wochenschr.* 1891, xxviii. 1130-1132.—131 Lundie, R. A. "The Treatment of Myxœdema," *Edinb. M. J.* 1892-93, xxxviii. 996-1005, 1 tab.—132. *Idem.* "A Case of Myxœdema treated by Thyroid Extract and Thyroid Feeding," *Brit Med. Journ.* 1893, i. 64.—133. Lunn, J. R. "A Larynx from a Myxœdema Female Patient," *Tr. Path. Soc. Lond.* 1888-90, xli. 32.—134. M'Gregor, G. W. "Myxœdema," *Columbus M. J.* 1896, xvii. 151-156.—135. Mackenzie, H. W. G. "A Case of Myxœdema treated with great Benefit by Feeding with fresh Thyroid Glands," *Brit. Med. Journ.* 1892, ii. 940.—136. *Idem.* "The Treatment of Myxœdema," *Lancet*, 1892, ii 999.—137. *Idem.* "Clinical Lecture on Myxœdema and the recent Advances in its Treatment," *Lancet*, 1893, i. 123-25.—138. *Idem.* "A Case of Myxœdema associated with Tubercular Disease of the Lungs and Larynx," *Trans. Path. Soc. Lond.* 1891-92, xliii. 184.—139 Macpherson, J. ["Treatment in Myxœdema"] *Trans. Med.-Chir. Soc. Edinb.* 1891-92, n.s. x. 99-103.—140. *Idem.* "Notes on a Case of Myxœdema treated by Thyroid Grafting," *Edinb. Med. Journ.* 1891-92, xxxvii. 1021-24.—141. Marie, P., and G[illegible]erlain, L. "Sur un cas de guérison de myxœdème par l'ingestion du glande thyroide du mouton, et sur les accidents qui peuvent survenir au cours de traitement thyroidien," *Bull. et mém. de soc. méd. des hôp. de Paris*, 1894, 3 s. xi. 83-87.—142. Marie, P. "Présentation d'une myxœdémateuse guérie par l'ingestion des glandes thyroides de mouton," *Bull. et mém. soc. méd. des hôp. de Paris*, 1894, 3 s. xi. 334-336.—143. *Idem.* "Rectification au sujet du cas de myxœdème traité par le Dr. Canter et présenté à la société des hôpitaux dans la séance du 18 mai 1894," *Bull. et mém. soc. méd. des hôp. de Paris*, 1894, 3d s. xi 371.—144. Marner, G. P. "Myxœdema," *Proc. Kansas Med. Soc.* Topeka, 1894, xxviii. 113-24.—145. Marr, H. C. "A Case of Myxœdema treated with Thyroid Feeding and Thyroid Extract," *Glasgow Med. Jour.* 1893, xl. 125-28.—146. Meltzer, S. J. "Ueber Myxodem," *N. Yorker med. Monatschr.* 1894, vi. 135-54.—147. *Idem.* "Myxœdema," *Med. Age*, Detroit, 1896, xiv. 129-32. —148. Mendel, E "Ein Fall von Myxodem," *Deutsche med. Wochenschr.* Leipz. u. Berl. 1893, xix. 25 —149. *Idem.* "Drei Falle von geheiltem Myxodem," *Deutsche med. Wochenschr.* Leipz. und Berl. 1895, xxi. 101-3.—150 Merklen, P., and C. Walther. "Sur un cas de myxœdème amélioré par la greffe thyroidienne," *Bull. et mém. soc. méd. des hôp de Par.* 1890, 3 s. vii. 859-70.—151. Miljanich, P. ["Case of Myxœdema"] *Med. Obozr. Mosk.* 1890, xxxiv. 493-95.—152. Miller, A. C. "Case of Myxœdema cured by Thyroid Feeding," *Edinb. Med. Journ.* 1893-94, xxxix. 215-19, 2 pl.—153. Miller, H T. "Failure of Thyroid Extract in a Case of Myxœdema," *Med. Rec.* N.Y. 1895, xlviii 24.—154. Mosler. "Ueber Myxodem," *Therap. Monatsh.* Berl. 1891, v. 461.—155. *Idem.* "Ueber das Myxoedem," *Verhandl. d. x. Internat. Med. Cong.* 1890, Berl. 1891, ii. 5, Abth. 134-38.—156. Murray, G. R. "Remarks on the Treatment of Myxœdema with Thyroid Juice," *Brit. Med. Journ.* 1892, ii. 449-51.—157. *Idem.* "The Treatment of Myxœdema and Cretinism," *Lancet*, 1893, i. 1130-32.—158. *Idem.* "After-history of the First Case of Myxœdema cured by Thyroid Extract," *Brit. Med. Journ.* 1895, i. 334. —159. Napier, A. "Notes of a Case of Myxœdema treated by Means of Subcutaneous Injections of an Extract of Sheep's Thyroid," *Glasgow M. J.* 1892, xxxviii. 161-65, 1 chart, 1 pl.—160. *Idem.* "Diuresis an increased Excretion of Urea in the Thyroid Treatment of Myxœdema," *Lancet*, 1893, ii. 805.—161. *Idem.* "Patient who had recovered from Myxœdema under Thyroid Treatment; Reference to six other Cases similarly treated successfully," *Trans. Glasgow Path. and Clin. Soc.* 1893-95, v. 104-122.—162. *Idem.* "Seven Cases of Myxœdema treated by Thyroid Feeding," *Glasgow Med. Journ.* 1894, xlii. 81-99.—163. Nielson, L. "Ein Fall von Myxodem durch Futterung mit glandulae thyreoidea (von Kalbern) geheilt, nebst einer Hypothese uber die physiologische Funktion dieser Druse," *Monatsh. f. prakt Dermat.* Hamb. 1893, xvi. 403-15.—164 *Idem.* "Behandlung af Myxodem med. Pil. glandulae thyreoideae siccatae," *Hosp.-Tid* Kjobenh. 1893, 4 R i. 1189-98; transl. *Monatshefte f. prakt. Dermat.* 1894, xviii. 115-25.—165. Northrup, W. P. "Infantile Myxœdema (two cases)," *Archives of Pediatrics*, New York, 1894, xi 793-801, 1 plate.—166. Oddo, C. "Un nouveau cas d'idiotie myxœdémateuse traité avec succès par la méthode thyroidienne," *Marseille méd.* 1895, xxxi. 193-210.—167. Oliver, T. "Myxœdema," *Internat Clin.* Phila. 1892, 2nd s. ii. 8-20, 2 pl. 1 diagram.—168. Oppenheimer, A. R. "Myxœdema and Exophthalmic Goitre in Sisters, with Remarks on the Symptomatology of the latter Disease," *Journ. Nerv. and Ment. Dis.* N.Y. 1895, xxii. 213-22; *Johns Hopkins Hosp. Bull.* Balt. 1895, vi. 33-35. —169. Ord, W. M. "Recent Cases of Myxœdema," *St. Thomas's Hosp. Rep.* 1889-90, Lond. 1891, n.s. xix. 125-135, 1 pl.—170. *Idem.* "Ueber das Myxoedem," *Verhandl. d. x. Internat. Med. Cong.* 1890, Berl. 1891, ii. 5 Abth. 132-134.—171. Ord, W. M., and E. White. "Clinical Remarks on certain Changes observed in the Urine in Myxœdema after the Administration of Glycerine Extract of Thyroid Gland," *Brit. Med Journ.* Lond. 1893, ii. 217.—172. Osler, W. "An Acute Myxœdematous Condition occurring in Goitre," *Johns Hopkins Hosp. Bull.* Balt. 1892, iii. 42.—173. Owen, J. L "A Case of Myxœdema, treated by Thyroid Extract," *Sheffield Med. Journ.* 1892-3, i 315.—174. Paget, Sir J. "Swellings above the Clavicle," in his *Stud. Old Case-books*, Lond. 1891, 136-138.—175. Pasteur, W. "A Case of Myxœdema treated by Raw Thyroid Glands and Fresh Thyroid Extract, in which severe Constitutional Symptoms developed under Treatment," *Trans. Clin. Soc. Lond.* 1892-3, xxvi. 230-234.—176. *Idem.* "Du traitement du myxœdème par les préparations thyroidiennes," *Revue méd. de la Suisse romande*, 1894, xiv. 35-50.—177. *Idem.* "Myxœdema," *Middlesex Hosp. Reports* (1892), 1894, 72-74.—178. Pel, P. K. "Myxodema," *Samml. klin. Vortr.* N.F. Leipz. 1895, No. 123. (*Innere Med.* No. 36, 255-288, 2 pl.)—179 Peli, G. "L' idiotismo mixedematoso," *Boll. d. sc. med. di Bologna*, 1891, 7 s. ii 163-174.—180. Poncet, A. "Thyroido-éréthisme chirurgical pour myxœdème et perversion mentale," *Mercredi méd.* Par. 1893, iv. 465.—181. Porteous, J. L. "Myxœdema, its History, Etiology, Pathology, and Treatment, with Particulars of a Case successfully treated," *Amer. Therap.* N.Y. 1893-4, ii. 1-9. —182. Putnam, J. J. "Cases of Myxœdema and Acromegalia treated with Benefit by Sheep's Thyroids. Recent Observations respecting the Pathology of the Cachexias following Disease of the Thyroid, Relationship of Myxœdema, Graves' Disease, and Acromegalia," *Trans. Assoc. Amer.*

Physicians, Phila. 1893, viii. 333-360.—183. Pye-Smith, R. J. "A Case of Myxœdema; with Microscopical Examination of Thyroid Body by A. J. Hall," *Sheffield Med. Journ.* 1892-3, i. 35-41, 1 pl.—184. Raven, T. F. "Myxœdema treated with Thyroid Tablets," *Brit. Med. Journ.* 1894, i. 12.—185. Régis, E. "Un cas type de myxœdème congénital (crétinisme sporadique) au début de traitement thyroidien," *Mém. et bull. soc. de méd. et chir. de Bordeaux* (1894), 1895, 763-70.—186. *Idem.* "Nouveau cas de myxœdème infantile notablement amélioré par le traitement thyroidien," *Journ. de méd. de Bordeaux*, 1895, xxv. 254; *Gaz. d. hôp. de Toulouse*, 1895, ix. 148.—187. *Idem.* "Un cas type de myxœdème congénital amélioré par le traitement thyroidien," *Mém. et bull. soc. de méd. et chir. de Bordeaux* (1895), 1896, 90-93.—188. *Idem.* "Nouveau cas de myxœdème infantile notablement amélioré par le traitement thyroidien," *ibid.* 263-267.—189. Rehn, H. "Ueber die Myxodemform des Kindesalters und die Erfolge ihrer Behandlung mit Schilddrusenextract," *Verhandl. d. Cong. f. innere Med.* Wiesb. 1893, xii. 224-229.—190. *Idem.* "Ueber cachessia thyreopriva congenita und deren Behandlung mit Schilddrusenextract nach einjahrige Beobachtung an zwei Kindern," *Atti d. xi. Congr. Med. Internaz. Roma*, 1894, iii. Pediat. 54.—191. Rennie, G. E. "Myxœdema," *Australasian Med. Gazette*, 1894, xiii. 2-6.—192. Robin, A., and E. Sereddé. "Observation d'un cas de myxœdème," *Ann. de dermat. et syph.* Par. 1892, 3 s. iii. 701-704.—193. *Idem.* "Observation d'un cas de myxœdème," *Bull. soc. franç. de dermat. et syph.* Par. 1892, iii. 303-306.—194. Robin, V. "Myxœdème congénital traité par des injections hypodermiques de suc thyroidien et par la greffe des corps thyroides," *Gaz. hebd. méd.* Par. 1892, 2 s. xxix. 451-453.—195. Rogers, J. K. P. "Myxœdema successfully treated by desiccated Thyroids," *Trans. Maine Med. Assoc.* Portland, 1895, xii. 166-72.—196. Roque. "Myxœdème chez une jeune fille," *Lyon méd.* 1893, lxxii. 615-618.—197. Sacchi, E. "Di un caso di mixedema operativo curato con successo col trattamento tiroides," *Riv. sper. di freniat.* Reggio-Emilia, 1894, xx. parte ii. 182-92, 1 plate.—198. Saundby, R. "Case of Myxœdema treated by Thyroid Gland," *Birming. Med. Rev.* 1893, xxxiii. 278-283.—199. Schmidt, J. J. "Ueber Myxodembehandlung; Vorstellung von spontanem Myxodem mit Zwergwuchs," *Deutsche med. Wochen.* Leipz. u. Berlin, 1894, xx. 806-809.—200. Schneider, Alfred. *Die Zusammensetzung des Blutes der Frauen verglichen mit derjenigen der Manner, nebst einer Analyse des Blutes dieser an Myxoedem erkrankten Frauen*, Dorpat, 1891, C. Mathiesen, 35 pp.—201. Schotten, E. "Ueber Myxodem und seine Behandlung mit innerlicher Darreichung von Schilddrusensubstanz," *Munchen med. Wochenschr.* 1893, xl. 981, 1002.—202. Shapland, J. D. "The Treatment of Myxœdema by Feeding with the Thyroid Gland of the Sheep," *Brit. Med. Journ.* 1893, i. 738.—203. Sinkler, W. "Myxœdema and its Treatment by Thyroid Extract," *Philad. Policlinic*, 1894, iii. 141-143.—204. Smith, T. F. H. "Enlarged Thyroid; Disappearance of Gland followed by Myxœdema," *Brit. Med. Journ.* 1896, i. 14.—205. Smith, J. L. "Myxœdema and the Thyroid Gland," *Med. Mag.* Lond. 1893-4, ii. 124-134.—206. Snowball, W. "Sequel of a Case of Congenital Myxœdema," *Intercolon. Quart. Journ. Med. and Surg.* Melbourne, 1894, i. 269.—207. Sonnenburg. "Acutes operatives Myxoedem behandelt mit Schilddrusenfutterung," *Verhandl. d. deutsch. Gesellsch. f. Chir.* Berl. 1894, xxiii. 497-503; [Discussion] pt. i. 169; *Archiv fur klin. Chirurgie*, Berl. 1894, xlviii. 857-63.—207*a*. Stalker, A. M. "Case of Myxœdema," *Lancet*, 1891, i. 82.—208. Stansfield. "A Case of Myxœdema with restless Melancholia treated by Injections of Thyroid Juice; recovery," *Brit. Med. Journ.* Lond. 1892, ii. 451.—209. Starr, M. A. "A Contribution to the Subject of Myxœdema, with the Report of Three Cases treated successfully by Thyroid Extract," *Med. Rec.* N.Y. 1893, lxiii. 705-708.—210. *Idem.* "A Contribution to the Subject of Myxœdema with the Report of Three Cases treated successfully by Thyroid Extract," *Tr. Assoc. Amer. Physicians*, Philad. 1893, viii. 361-371.—211. Steiner. "Ueber Myxodem," *Deutsch. med. Wochnschr.* Leipz. 1891, xvii. 1070-1072.—212. Stewart, G. "The Treatment of Myxœdema by Thyroid Feeding, its Advantages and Risks," *Practitioner*, Lond. 1893, li. 1-8.—213. Thomson, J. "On a case of Myxœdematoid Swelling of One-half of the Body in a Sporadic Cretin," *Edinb. Med. Journ.* 1891-2, xxxvii. 249-253, 1 pl.—214. *Idem.* "Note on a Case of Myxœdema which ended fatally shortly after the Commencement of Thyroid Treatment," *Edinb. Med. Journ.* 1892-3, xxxviii. 1014-1018.—215. Thompson, W. G. "Report of a Case of Myxœdema," *Med. Rec.* N.Y. 1893, xliv. 174.—216. *Idem.* "Report of a Case of Myxœdema," *Trans. Assoc. Amer. Physicians*, Philad. 1893, viii. 372-379.—217. Thibierge, G. "De la cachexie pachydermique, ou myxœdème," *Gaz. d. hôp.* Par. 1891, lxvi. 117-126.

—218. *Idem.* "De la cachexie pachydermique, ou myxœdème," *Gaz. d. hôp. de Toulouse*, 1891, v. 42, 51, 59, 67, 76, 84.—219. Tresilian, F. "A Fatal Case of Myxœdema," *Med. Press and Circ.* Lond. 1895, n.s. lix. 270.—220. Vallin, E. "Le traitement culinaire du myxœdème," *Rev. d'hyg.* Par. 1893, xv. 478-486.—221. Vermehren, F. "Stoffwechselweitersuchungen nach Behandlung mit Glandula thyreoidea an Individuen mit und ohne Myxödem," *Deutsche med. Wochnschr.* Leipz. u. Berl. 1893, xix. 1037.—222. *Idem.* "Sul trattamento del mixoedema," *Gazz. d. osp.* Milano, 1893, xiv. 275.—223. *Idem.* "Ueber die Behandlung des Myxödems," *Deutsche med. Wochnschr.* Leipz. u. Berl. 1893, xix. 255-257.—224. *Idem.* "Om Myxoedembehandling," *Hosp.-Tid.* Kjobenh. 1893, 4 R. i. 125-132.—225. *Idem.* "Nogle Bemaerkninger om Behandlingen af Myxoedem," *Hosp.-Tid.* Kjöbenh. 1893, 4 R. i. 389-391.—226. Vinton, Maria M. "A Case of Myxœdema," *Med. Rec.* N.Y. 1892, xli. 250.—227. Voisin, J. "Idiotie myxœdémateuse améliorée par la greffe thyroidienne et par l'alimentation thyroidienne," *Bull. et mém. soc. méd. d. hôp. de Paris*, 1894, 3 s. xi. 187-89.—228. Wessinger, J. A. "Myxœdema, with Photographic Illustrations," *Trans. Michigan Med. Assoc.* Detroit, 1894, xviii. 232-36, 1 plate.—229. Whitwell, J. R. "The Nervous Element in Myxœdema," *Brit. Med. Journ.* 1892, i. 430-432.—230. Wichmann, R. "Ein Fall von Myxödem, gebessert durch Injectionen mit Schilddrüsensaft," *Deutsche med. Wochnschr.* Leipz. u. Berl. 1893, xix. 26-28. —231. *Idem.* "Weitere Mittheilungen über Myxodem," *Deutsche med. Wochenschr.* Leipz. u. Berl. 1893, xix. 259.—232. Wilson, A. Marius. *Myxœdema and the Effects of Climate on the Disease*, Lond. 1894, Scientific Press, 36 pp.

The Functions of the Thyroid Gland:—1. Baber, C. *Philosophical Transactions*, 1876 and 1881.—2. Baumann, E. Hoppe-Seyler's *Zeit. f. phys. Chemie*, vol. xxi. p. 319.—3. Horsley, Victor. "Report on Myxœdema," *Trans. Clin. Soc. Lond.* 1888; "Physiology and Pathology of Thyroid Gland," *Brit. Med. Journ.* vol. ii. 1896, pp. 16-23.—4. Hutchison, R. "On the Active Constituent of the Thyroid Gland," *Brit. Med. Journ.* vol. i. 1897, p. 194.—5. White, E. "The Pharmacy of the Thyroid Gland," *Pharmaceut. Journ.* 2nd Sept. 1893.

The Parathyroid Glands:—1. Edmunds. *Trans. Path. Soc. Lond.* 1895, 1896; and *Journ. Path. and Bacter.* Jan. 1896.—2. Gley. *Arch. de physiol. norm. et path.* 1892 and 1893.—3. Horsley. *Brit. Med. Journ.* Dec. 1896.—4. Kohn. *Arch. f. mikrosk. Anat.* Bd. 44, H. 3, 1895.—5. Sandström. "Ueber eine neue Drüse beim Menschen und bei verschiedenen Saugethieren," *Schmidt's Jahrb.* 1880.—6. Vassale and Generali. *Riv. di Patol. nerv. e ment.* March and July 1896.

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SPORADIC CRETINISM

(CONGENITAL MYXŒDEMA, OR MYXŒDEMA OF CHILDHOOD)

Definition.—A state allied to endemic cretinism and to myxœdema; occurring in countries and districts where the malady is not endemic; associated with imperfect development both of the intellect and of the body, and due to congenital absence of the thyroid gland, or to want of function in this organ.

Causation. — The conditions of the origin of sporadic cretinism are unknown. Some cases have been ascribed to consanguinity between the parents; others to a family history of alcoholism, or of tubercular or syphilitic disease. Others, again, have been attributed to mental shock or worry on the part of the mother during pregnancy. There is sometimes a family history of "deformities." But in the large majority of the cases recorded the mode of causation is obscure, the subjects of this disease being members of large and otherwise healthy families.

Description.—The condition is rarely observed before the completion of the second year, as no serious symptoms are noticeable before that time; and, if any difference from the normal be noted, it is usually regarded merely as "backwardness." The disease is, however, quite recognisable, at all events, as early as the tenth month, when the main features may be as follows:—The child is stunted in growth, there is a great want of due proportion between the various parts of the body, the growth of the trunk and limbs not keeping pace with that of the head, hands, and feet. The face is broad and expressionless; the eyes dull, and situated far apart at the ends of a furrow running across the root of the nose. The nose is broad, with flattened extremity, like that of a negro; the lips coarse, protruding, and gaping, give a glimpse of a swollen tongue appearing between two rows of carious teeth. There is usually well-marked salivation. The head hangs forward on the chest, the erector muscles being too weak to support its weight. In this way an antero-posterior curvature of the cervical and upper dorsal vertebræ is often established, the convexity being directed backwards so as to give rise in some cases to suspicion of spinal disease. In well-marked cases there is usually a complementary curvature of the lumbar spine, increasing the projection of the abdomen; a characteristic feature which is one of the last to disappear under treatment. The limbs are short, the legs are often bowed in a manner suggestive of rickety deformity, and occasionally require operative treatment; there may be some epiphyseal enlargements also. The skin is yellow and leathery, and is rough to the touch; it is loose, and often hangs in folds over the abdomen. In some cases there is a total absence of perspiration; but this symptom is not constant, as in myxœdema. The hair is scanty and stunted, owing to its extreme brittleness: its appearance resembles a poor crop of wheat after a storm; and to the touch it is harsh, with a dry quality of harshness which almost suggests heat. The scalp is dry and scurfy. Usually there is nothing to be felt in the region of the thyroid gland, but the gland may be present, even indeed in an enlarged form. In many cases there are large lobulated fatty masses situated between the sterno-mastoids, above the clavicles, and in the armpits; they are not, as a rule, symmetrical. The temperature is subnormal, and the patients are extremely sensitive to cold. The urine usually is passed in large quantity, contains no albumin, and presents a marked diminution of urea; but in a certain number of cases the urea has been found decidedly increased. The blood exhibits little change in its corpuscular elements; there is no leucocytosis, but there is a marked diminution in the quantity of hæmoglobin, the defect amounting to 50 and even 60 per cent.

There is a great variety in the mental condition of patients suffering from this disease. In the most favourable cases, although the patient remains dwarfed as he grows up, he is capable of attending to housework and of following some light employment. On the other hand, he may remain absolutely imbecile, a mere log. In the majority of cases a medium state exists. The patient is dull, and is roused with difficulty, but can be made to recognise external objects to a certain extent; he especially enjoys dainties; sensation is retarded, and all movements are begun with difficulty, and are slow and deliberate—the gait especially so. The temper, as a rule, is placid; but it may be varied by fits of passion and of despondency. A certain number of patients are spiteful and vicious. The habits are usually dirty, and even at the age of six or eight years the patient is often unable to feed himself. The difference between the real and the apparent age becomes more noticeable as time goes on, patients of twenty years of age or over having the size and general appearance of young children.

Pathology and morbid anatomy.—The thyroid gland is absent in the majority of cases, being represented merely by a few fatty granules. In other cases it has undergone cystic or fibro-cystic degeneration.

The cranial bones are thickened and the diploe diminished. Premature synostosis of the spheno-basilic suture has been described by Virchow. The brain is small, and there is an increase of intraventricular and subarachnoid fluid. The long bones, with the exception of the clavicle, are shortened, and often present a curious cupping at the extremities which, embracing the epiphyses, gives rise to an appearance of epiphyseal enlargement. There are no peculiar visceral lesions.

Diagnosis.—The various forms of idiocy unassociated with thyroid affection, and rickets must be distinguished from this disease. The condition of the hair, skin, and teeth and the presence of the thyroid will mark the former class, the absence of mental symptoms the latter.

Prognosis.—Under the thyroid treatment this is eminently favourable. Suitably conducted, it will certainly ensure rapid and complete bodily improvement, and though, as we shall see presently, mental improvement is not invariable, it is even more remarkable when it occurs. The earlier in life the treatment is begun the more complete and lasting appear to be the results. In all probability, however, the treatment in some form will have to be persisted in throughout the life of the patient.

Treatment.—Previous to the experiments of Murray and Mackenzie little could be done to alleviate this disease. Several German surgeons, notably Boccher, and in this country Victor Horsley, Clutton, and others had tried the implantation, either in the abdominal cavity or beneath the skin, of portions of thyroid glands of sheep, or of parenchymatous bronchoceles from human subjects. The effect, though favourable, was transitory, and disappeared with the absorption of the implanted tissue. In 1892, Dr. Murray showed that subcutaneous injection of an extract of the thyroid gland caused alleviation of symptoms, and, later, Dr. Mackenzie showed that feeding by the mouth was equally efficacious. The gland is best administered in the form of a dried extract, either as a powder, or in the form of a tablet. The dose should be small at first, beginning with three grains a day, and should be carefully increased in amount until the full effect is obtained. Then large doses must be kept up until what may be called a cure is obtained. Then only a sufficient dose, which varies according to the individual, should be given to maintain the proper condition of health. The effect of the treatment in cases of sporadic cretinism resembles closely that which obtains in myxœdema; but there are some considerable differences. In the first place, there is as a rule a complete absence of the symptoms of discomfort due to the treatment which are so often noted in the adult disease. On the other hand, symptoms of improvement do not occur so soon as in cases of myxœdema, no change of any importance being noted in the first week. First, there appears a marked decrease in the body-weight, accompanied by a decided decrease in bulk. This is accompanied by increased diaphoresis, an improvement in the condition of the skin and hands, an increased activity of movement, and a brightening of expression. Where diminished before, the quantity of urea excreted approaches the normal. The quantity of hæmoglobin rapidly increases, with a corresponding diminution of pallor. After a period of loss the body-weight begins to ascend, and this is the most trustworthy sign of the approach to a "cure." When the body-weight corresponds fairly well to the height of the child, the quantity of thyroid extract given may be gradually diminished, until the smallest dose compatible with health is reached. This in each case must be a matter of experience. Overdose, or a prolonged course of large doses, may induce symptoms of irritability and other troubles suggesting Graves' disease. It is interesting to note that where treatment is begun before the period of second dentition, however badly decayed the first set may have been, the second set of teeth are large and strong. Bodily growth is in some cases remarkably rapid, as much as 5½ inches in one year having been recorded. Mental improvement varies considerably in degree. In some cases, even where there has been a marked degree of hebetude at first, the children after a time become equal in intelligence to their contemporaries, and are able to rival them at their studies. In other cases, although the bodily improvement is remarkable, the mental condition remains absolutely unimproved. There are various stages between these two extremes.

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REFERENCES

1. ALLARA, VINCENZO. *Sulla causa del cretinesimo; studio.* Milano, 1892, C. Chiesa and F. Guindani, 419 pp. 2 tab. — 2. *Idem.* *Der Kretinismus, seine Ursachen und seine Heilung, Studie:* autorisierte Uebersetzung aus dem Italienischen von Hans Merian. Leipzig, 1894, W. Friedrich, 396 pp. 2 tab. — 3. ALLEN, H. "Demonstration of Skulls showing the Effects of Cretinism on the Shape of the Nasal Chambers," *Trans. Amer. Laryngol. Assoc.* 1894, New York, 1895, xvi. 142-68.—4. ANSON, G. E. "Result of a Year's Treatment of a Case of Sporadic Cretinism by Thyroid Juice," *Lancet*, 1094, i. 1863.—5. BEADLES, C. F. "The Treatment of Myxœdema and Cretinism, being a Review of the Treatment of those Diseases by Thyroid Gland, with a Table of 100 published Cases," *Journ. Ment. Sc.* London, 1893, xxxix. 343, 509, 622, 1 pl.—6. BLAKE, E. T. *Myxœdema, Cretinism and the Goitre, with some of their Relations.* Bristol, 1894, 89 pages, 5 plates. — 7. BRAMWELL, B. "Sporadic Cretinism," *Atlas of Clin. Med.* fol. Edinb. 1891, ii. pt. 1, 17-27, 2 pl.—8. *Idem.* "Clinical Remarks on a Case of Sporadic Cretinism," *Brit. Med. Journ.* 1894, i. 6-11.—9. *Idem.* "Clinical Remarks on a Case of Sporadic Cretinism," *Trans. Med.-Chir. Soc. Edinb.* 1894, n.s. xiii. 34-45. — 10. CARMICHAEL, E. "Cretinism treated by the Hypodermic Injection of Thyroid Extract and by Feeding," *Lancet*, 1893, i. 580.—11.

"Congenital Cretinism," *Clinical Sketches*, London, 1895, ii. 33-35.—12. DERCUM, F. X. "A Case of Sporadic Cretinism," *Philad. Hosp. Rep.* 1893, ii. 157, 1 plate.—13. DOLEGA. "Ein Fall von Cretinismus beruhend auf einer primaren Hemmung des Knochenwachsthums," *Beitr. z. path. Anat. u. z. allg. Path.* Jena, 1890, ix. 488-514.—14. FINLAYSON. "Case of a Cretin Child under Thyroid Treatment," *Glasgow M. J.* 1896, xlv. 378-382.—15. GARROD, A. G. "Case of a Cretin under Thyroid Treatment," *Trans. Med. Soc. Lond.* 1894-95, xviii. 368.—16. HAGAN, H. "A Case of Cretinism," *Atlanta M. and S. J.* 1892-3, n.s. ix. 705-707 —17. HASKOVEC, L. "Ein Fall von sporadischen Cretinismus behandelt mit einem Schilddrusenpraparat," *Wiener med. Wochenschr.* 1895, xlv. 1805, 1857.—18. HELLIER, J. B. "A Case of Sporadic Cretinism treated by Feeding with Thyroid Extract," *Lancet*, 1893, iii. 1117.—19. IRELAND, W. W. "On Sporadic Cretinism," *Edinb. Med. Journ.* 1892-3, xxxviii. 1018-1022.—20. KIRK, R. "Death of a Cretin aged Twenty Years," *Lancet*, 1893, i. 524.—21. KOCHER, T. "Zur Verhutung des Cretinismus und cretinoider Zustande nach neuen Forschungen," *Deutsche Zeitschr. f. Chir.* xxxiv. Festschr. . . C. Thiersch, etc. Leipzig, 1892, 556-626, 1 plate.—22. LEECH, P. "A Case of Sporadic Cretinism treated by Tabloids of Thyroid Gland," *Quarterly Med. Journ.* Sheffield, 1893-94, ii. 320-22, 1 plate.—23. LLOYD, J. H. "Sporadic Cretinism," *Internat. Clin.* Phila. 1892, 2nd s. ii. 113-117, 1 pl.—24. LUNN, J. R. "A Case of Female Cretin treated by the Administration of Sheep's Thyroid," *Trans. Med. Soc. Lond.* xvii. 1894, p. 330.—25. MIDDLETON. "A Case of Sporadic Cretinism," *Glasgow Med. Journ.* 1896, xlv. 127-30. —26. MURRELL, G. F. "A Case of Sporadic Cretinism treated by Thyroid Juice," *St. Barthol. Hosp. Rep.* 1893, xxix. 101-103.—27. NESS, B. "Case of Sporadic Cretinism," *Glasgow Med. Journ.* 1896, xlv. 125-27.—28. NOYES, W. B. "A Study of Sporadic Cretinism," *N. York M. J.* 1896, lxiii. 334-341 ; *Nerve and Ment. Dis.* N.Y. 1896, xxiii. 312-315.—29. OSLER, W. "On Sporadic Cretinism in America," *Amer. Journ Med. Sci.* 1893, n.s. cvi. 503-518.—30. *Idem.* "On Sporadic Cretinism in America," *Trans. Assoc. Amer. Physicians*, Phila. 1893, viii. 380-398.—31. *Idem.* "Case of Sporadic Cretinism (Infantile Myxœdema) treated successfully with Thyroid Extract," *Archives of Pediatrics*, 1895, xii. 105-108.—32. OTTOLENGHI, S. "Il campo visivo nei cretini," *Arch. di psichiat. etc.* Torino, 1893, xiv 256-263, 1 pl.—33. PARKER, W. R. "A Goitrous Cretin under Thyroid Extract," *Brit. M. J.* Lond. 1896, i. 1550-1552.—34. *Idem.* "A Cretin treated by Thyroid Extract," *Brit. Med. Journ.* 1896, i. 333.—35. PATERSON, G. A. "A Case of Sporadic Cretinism in an Infant ; Treatment by Thyroid Extract," *Lancet*, 1893, ii. 1116.—36. RAILTON, T. C. "Sporadic Cretinism," *Brit. Med. Journ.* Lond. 1891, i. 694 —37. *Idem.* "Sporadic Cretinism treated by Administration of the Thyroid Gland," *Brit. Med. Journ.* 1894, i. 1180.—38. SINKLER, W. "Sporadic Cretinism and its Treatment by Thyroid Extract," *Internat. Med. Mag.* Philad. 1894-95, iii. 785-93, 1 plate.—39. SMITH, T. "Case of Sporadic Cretinism treated with Thyroid Gland," *Brit. Med. Journ.* 1894, i. 1178-80.—40. SMITH, T. T. "Cases of Sporadic Cretinism treated by Thyroid Extract," *Journ. Mental Science*, Lond. 1895, xli. 280-89, 4 plates.—41. SYMINGTON, J., and H. A. THOMSON. "A Case of Defective Endochondral Ossification in a Human Fœtus (so-called Cretinoid)," [From *Proc. Roy. Soc. Edinb.* xviii.] *Rep. Lab. Roy. Coll. Physic. Edinb.* Edinb. and Lond. 1892, iv. 237-254.—42. THOMSON, J. "Further Notes of a Case of Sporadic Cretinism treated by Thyroid Feeding," *Edinb. Med. Journ.* 1893-94, xxxix. 720-23, 1 plate.—43. *Idem.* "Further Notes of a Case of Sporadic Cretinism treated by Thyroid Feeding," *Trans. Med.-Chir. Soc. Edinb.* 1894, n.s. xiii. 65-68, 4 plates.—44. *Idem* "On a Mild Case of Cretinism and its Progress under Thyroid Treatment," *Edinb. Hosp Reports*, 1894, ii. 252-57, 1 plate.—45. *Idem.* "A Case of Sporadic Cretinism (Cretinoid Idiocy) with an Œdematous or (?) Myxœdematoid Condition of the Right Side of the Body," *Tr. Med.-Chir. Soc. Edinb.* 1889-90, n.s. ix. 145.—46. TOWNSEND, C. W. "A Case of Sporadic Congenital Cretinism," *Arch. Pediatrics*, N.Y. 1892, ix. 825-829. —47. VARIOT, G. "Un cas de crétinisme sporadique," *Journ. de clin. et de thérap. infantile*, Paris, 1895, iii. 741-744.—48. VINKE, H. H. "Sporadic Cretinism, with Report of a Case treated with Thyroid Gland," *Med. News*, New York, 1896, lxviii. 309-13.—49. VOROTYNSKI, B. T. ["Case of Sporadic Cretinism"] *Vestnik. Klin. i sudebnoi psichiat. i nervopatol.* St. Petersb. 1892, ii. 40-51.—50. WAGNER. "Untersuchungen uber den Cretinismus," *Jahrb. für Psychiatrie*, Leipzig u. Wien, 1893, xii. 102-137 ; 1894, xiv. 17-36.—51. *Idem.* "Ueber den Cretinismus," *Med.-Chir. Centralbl.* Wien, 1893, xxviii. 245-252.—52. *Idem.* "Ueber den Cretinismus," *Mitth. d. Ver. d. Aerzte in Steiermark*, Graz, 1893, xxx. 87-101.—53. WEST, J. P. "A Case of Congenital Cretinism," *Archives of Pediatrics*, New York, 1895, xii. 348-52, 2 plates.—54. WOOD, A. J. "Three Cases of Sporadic Cretinism," *Austral. Med. Journ.* Melbourne, 1893, n.s. xv. 165-175.—55. Bibliography of Myxœdema.

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GRAVES' DISEASE

Definition.—A disease characterised by enlargement of the thyroid gland, protrusion of the eyeballs, tachycardia and palpitation, and tremors of the extremities. With these may be associated a more or less profound disturbance of mental equilibrium, emaciation, sweating, anæmia, looseness of the bowels, and derangement of the catamenial function.

Etiology.—This disease mainly affects women between the ages of sixteen and forty years. Its incidence according to age is shown by the figures compiled by Buschan. Of 495 patients, 15 were under ten years of age, 352 were between sixteen and forty, 163 occurring between twenty and thirty, 69 were between forty and fifty, and 31 were over fifty. The disease is thus rare at the two extremes of life. Only about 30 cases altogether have been reported in children. The age of the youngest was two and a half years, a case which is recorded by Divel. Dr. Dreschfeld has observed a definite example in a child aged three.

The disease, though rare in men, may occur in them in a well-marked form. Its relative frequency in men and women has been very variously estimated. Buschan, who has collected 980 cases from the records, found 805 females to 175 males, a proportion of about nine to two. It is probable that cases in men are recorded more frequently than those in women on account of their comparative rarity; and thus the proportion of men to women, given by Buschan, may be too high. It is possible, too, that the proportion varies in different countries. Charcot speaks of the disease as being only a little less frequent in men than in women, and Eulenburg gives the proportion as one male to two females. Out of nearly a hundred cases of the malady personally observed by us, there have been only five cases in males. As with adults, the children attacked have been usually females—a contrast to our experience in cretinism.

The disease may occur in several members of the same family. It has been observed in three successive generations. Thus it has been recorded that two sisters, their father, and two of his sisters, and his mother were subjects of the malady. There is also Oesterreicher's well-known case where a hysterical woman had ten children, of whom eight suffered from exophthalmic goitre; and one of the latter had three children thus affected.

The malady is often consequent upon acute disease, fright or other severe mental shock, worry, prolonged mental strain, and over-fatigue. A good many cases appear to have dated from an attack of influenza.

Quinsy, rheumatism, and a tendency to bleeding, especially in the form of epistaxis, have been observed as antecedents in a significant number of cases.

Fright, intense grief, and other profound emotional disturbances have long been recognised as immediate causes of the disease. It is interesting to note the close connection between the acute or chronic symptoms of exophthalmic goitre and the more immediate effects of terror. The descriptions given by Darwin and Sir Charles Bell of the condition presented by persons under the influence of intense fear at once suggest the symptoms of exophthalmic goitre. The heart beats quickly and violently, so that it palpitates or knocks against the ribs. There is trembling of all the muscles of the body. The eyes start forward and the uncovered and protruding eyeballs are fixed on the object of terror; the skin breaks out into a cold and clammy sweat, and the face and neck are flushed or pallid. The intestines are affected.

Of all the emotions, fear is notoriously the most apt to induce trembling.

Protrusion of the eyes, as well as trembling, is mentioned by nearly all writers who describe the effects of horror or fear.

We have no knowledge that the thyroid gland ordinarily becomes enlarged under the influence of fear, but it is evident that the other chief features of exophthalmic goitre temporarily result from such emotion. That, occasionally, Graves' disease, in a well-marked form, rapidly follows a sudden shock to the nervous system, indicates that all the symptoms may be produced in such a way.

We think that these facts suggest that the thyroid condition is, at any rate, not the primary cause of the disease. We conclude that the disease depends on a derangement of the emotional nervous system, together with an altered perverted condition of the thyroid gland, which serves to keep up many of the characteristic symptoms.

We are bound to recognise that, as in the case of myxœdema, the large majority of the patients are of the female sex. It is well known that changes of a quasi-inflammatory nature occur in the body during disordered menstruation and during pregnancy.

The association of the disease with other nervous disorders in the patient, or in other members of the same family, has often been pointed out. Chorea, hysteria, epilepsy, diabetes, and insanity are some of the diseases with which it thus appears to have relations.

The connection of the malady with chlorosis is uncertain, but undoubtedly the latter frequently accompanies it in young women. Occasionally the disorder shows itself for the first time during pregnancy or after parturition. On the other hand, its symptoms may undergo amelioration during pregnancy. Disorders of menstruation sometimes precede the disease, and probably have some causal relation with it.

Some have looked on Graves' disease as an auto-intoxication; others regard it as reflexly excited by some local morbid condition in the nose or elsewhere.

The disease affects persons of all classes of society. It appears to be on the whole as prevalent in one country as another; but some localities furnish more cases than others. Thus certain parts of Kent, Surrey, Wiltshire, and the Thames valley have produced a relatively large proportion of the cases under our observation. In districts where ordinary goitre prevails, the exophthalmic form is also met with.

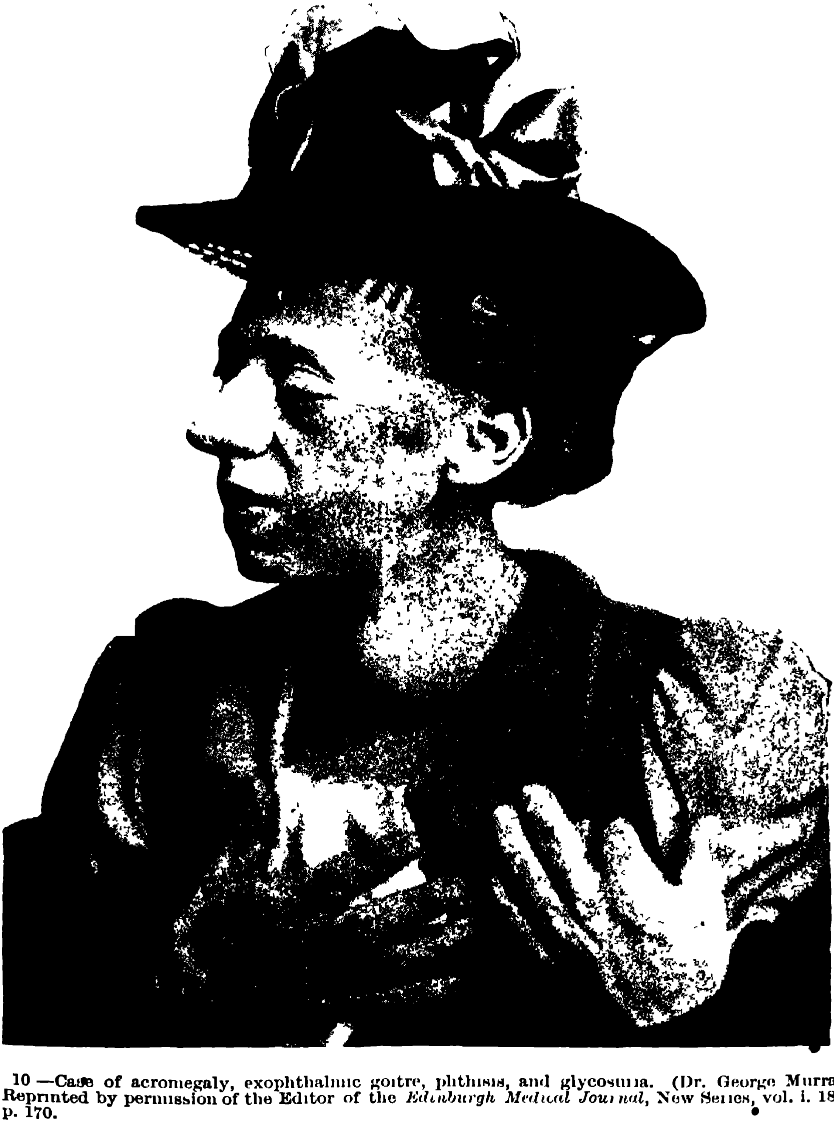

Fig. 10.—Case of acromegaly, exophthalmic goitre, phthisis, and glycosuria. (Dr. George Murray.) Reprinted by permission of the Editor of the *Edinburgh Medical Journal*, New Series, vol. i. 1897, p. 170.

Symptoms.—The symptoms mentioned in the definition as characteristic of the disease may come on simultaneously or may gradually appear one after the other. *The thyroid enlargement, together with the protrusion of the eyes, renders the disorder easy to recognise.* Sometimes the first sign of anything amiss is an alteration in temper, the patient being easily worried and extremely irritable. With this is soon associated functional disturbance of the heart. The thyroid enlargement has probably been present from the first, but may not be observed till a later period. The palpitation now increases and the eyes become prominent; the patient becomes more irritable and excitable, and is apt to have attacks of trembling.

We shall first proceed to consider the various symptoms in detail, and then discuss the varieties of the disease, its course and its duration.

The *thyroid enlargement* is usually moderate. In many cases the enlargement is uniform, but appears to be unsymmetrical, the right side being larger than the left. The reason of this apparent difference on the two sides is that, as a rule, the normal gland is not really symmetrical, the right lobe being larger than the left; and hypertrophy magnifies the disparity. In some cases the enlargement is irregular and the tumour may present local nodular swellings. The swelling is generally soft, but sometimes, especially when irregular, it is firm and hard. The latter is especially likely to be the case where a goitre has preceded the onset of the other symptoms of the disease.

The gland appears to pulsate in common with the vessels in the neck. On placing the hand over the goitre a thrill is often perceptible, and on applying the stethoscope a loud murmur is audible, like the venous hum in the neck in a case of anæmia.

During the course of the disease the goitre fluctuates in size. After slowly increasing for a time it may gradually diminish. In other cases it may repeatedly increase and diminish.

Often the patient has not noticed any enlargement of the thyroid until it is pointed out by the physician. In men, attention is sometimes first drawn to it by their collars becoming too tight.

The eyes.—The exophthalmos, like the thyroid enlargement, varies in amount in different cases. Occasionally the protrusion is so great that the eyelids cannot voluntarily be closed, nor do they meet in sleep. On the other hand, it may be so slight as to be hardly perceptible. In marked cases the eyeballs appear as if starting out of the head. In some cases nothing more than a slightly staring look may be noticed. The exophthalmos is often not quite equal on the two sides, and several purely unilateral cases have been reported. Two important signs have been described in connection with exophthalmos; these are known as Von Grafe's sign and Stellwag's sign.

Von Gräfe's sign consists in the lagging of the upper eyelid in downward movement of the eyes. To obtain it the finger or a pencil should be held horizontally in front of the patient's eyes, and she should be directed to follow it while it is gradually lowered. If the sign is present the upper eyelids lag, not closely following the movements of the eyeballs, so that the sclerotics may become visible between the lids and the corneæ. Von Grafe's sign is generally present in the disease, but it is sometimes observed in other conditions.

Stellwag's sign consists in an increase of the palpebral fissure due to retraction of the upper lid and diminished frequency and incompleteness of winking under reflex stimulation. In consequence of the retraction of the lids, the sclerotic may show all round the iris. The widening of the palpebral fissure is not a mechanical result of the exophthalmos, and is not directly in proportion to it. The diminished reflex excitability contributes to give the eyes their staring look. Stellwag's sign is usually present.

Mobius has drawn attention to another eye symptom, namely, insufficient power of convergence for near objects. On convergence the patients experience a sense of strain, but have no double vision. This is by no means a constant feature of the malady. A glistening, slightly œdematous condition of the conjunctivæ may frequently be noticed.

Occasionally some weakness of the external ocular muscles exists. Slight drooping of both upper eyelids has been observed. At times there is some weakness of the external recti, producing double vision on looking to the extreme right or left. In rare cases complete ophthalmoplegia externa has been recorded.

No defect of vision, as a rule, accompanies the exophthalmos. Besides the straining which sometimes accompanies convergence, patients often complain of various subjective symptoms, such as flashes of light before the eyes, and feelings as if the eyes were being pushed forwards.

Sometimes there is painful spasm of the orbicularis palpebrarum. Sometimes accompanying the spasm there is dislocation of the eyeball; but this, fortunately, is a rare event. Watering of the eyes is often a source of annoyance, but, on the other hand, there may be an abnormal dryness.

Ulceration of the cornea occasionally occurs, though rarely, and this may go on to perforation and destruction of the eye. In a case recently under the care of one of us, the perforation had occurred quite painlessly, and the eye was lost before the patient made any complaint about it.

Accompanying the protrusion of the eyeballs and the affections of the lids already mentioned, an œdematous swelling of the upper and sometimes also of the lower eyelids is not infrequently found. Sometimes the swelling is not a true œdema, as it can be dissipated by causing contraction of the orbiculares by electric stimulation. Sometimes the swelling remains for a long period, even after many of the other symptoms of the disease have disappeared.

Arching of the eyebrows is generally to be observed whenever exophthalmos is well marked.

The *disturbances of the circulation* form the most marked and constant features of the disease.

The heart's action is always increased in rapidity. The rate varies in the slighter cases between 90 and 100 beats in the minute, and in cases of ordinary severity between 100 and 130. In severe cases the heart may beat at the rate of 160 pulsations or even more in the minute.

The action is not merely persistently rapid, but it is apt to be increased on slight exciting causes.

The patients, as a rule, are painfully conscious of palpitation, and it is the chief trouble of which they complain. In some cases they have a feeling as if the heart were beating all over the body. Occasionally, however, there is a very rapid cardiac action without the patient being uncomfortably conscious of it.

The pulsation of the carotids in the neck is generally a very conspicuous feature of the disease. On inspection they can be seen beating forcibly and rapidly.

As a rule the action of the heart is regular; but it may become irregular, and this is most likely to be the case when the disease is progressing unfavourably.

Often the increased cardiac action is accompanied by cardiac hypertrophy or dilatation. Systolic murmurs at the base of the heart are not uncommon, while sometimes there is evidence of organic valvular disease.

As regards the radial pulse there is nothing constant in its character except its frequency. In different cases it is hard or soft, strong or weak.

Tremor is now recognised as one of the cardinal symptoms of the disease. It varies very much in degree. In one case it may be the chief trouble of which the patient complains, while in others its presence will only be recognised by the physician on careful examination. If a patient, the subject of this disease, be asked to stretch out her extended hands, a characteristic tremor will be observed, consisting of vibratory movements of small amplitude, with a period of about one-eighth or one-ninth of a second. The tremor is of the same nature as that which may be observed in over-fatigued muscles in healthy persons. The tremor is a communicated one, and affects the whole extremity, not the fingers only. It may be observed in the leg as well as in the arm. It usually affects both sides of the body, but in some cases it is limited to, or is very much more marked in one limb.

The tremor is generally more obvious when the patient is flurried, and sometimes may only be noticeable under such circumstances. It is more conspicuous when the patients are examined standing up than when they are lying down.

Besides the tremor which the physician observes on examination, the patients frequently themselves experience attacks of trembling which may affect the whole of the body, such attacks bearing the same relation to the tremor that palpitation does to the rapid cardiac action. It is, as a rule, only when the tremor is aggravated that it interferes with the movements of the hands, and then only the more delicate actions are affected, such as writing, sewing, or buttoning a glove or dress. The patient will probably use the spoon or fork or carry a cup to the lips with perfect steadiness. Trousseau remarked of one of his patients, that on account of trembling she was unable to sign her daughter's marriage contract.

We shall proceed now to describe the symptoms which are usually associated with those of more special diagnostic importance already described.

Emaciation is a very characteristic feature of all acute cases, or of those in which the disease is active. Sometimes the degree of emaciation is extreme, and when this is the case the prognosis is most unfavourable. A loss of two or three stones is not uncommonly seen. As the disease subsides the patient regains flesh. Mild cases are sometimes met with where the patients remain well nourished throughout.

Loss of strength is generally in proportion to the severity of the disease. Usually the patients are easily tired, but sometimes excitement will carry them through a great deal of exertion.

The temperature of the body, as a rule, is little elevated if at all. We have observed the temperature with great care in a large number of cases and find that a rise of temperature is quite exceptional. Some observers, however, have recorded febrile cases. Our belief is that, generally speaking, if fever is present it is due to some complication. Although the temperature may not be raised, *a subjective feeling of heat* is the rule. It is most troublesome at night when the patient is in bed, and even when the weather is cold she will feel warm with an amount of covering which a healthy person would consider quite insufficient. She likes cold weather and is very intolerant of heat.

Affections of the skin are of considerable interest and are not infrequent.

In the first place the patients often suffer from flushing of the head and neck, especially when under observation. At the same time they feel as if the blood were rushing to the head, and their face and neck become uncomfortably hot. These attacks, although worse under observation, often come on without apparent cause. The sweat-glands are generally over-active, and sweating may be much in excess. Sweating of the hands and feet may be a source of great annoyance to the patient. The increased moisture on the skin is no doubt the cause of the great diminution of the electrical resistance of the body observed by Vigouroux and Charcot.

Pigmentary changes in the skin are not uncommon. The complexion almost invariably suffers. The skin of the face and of other parts of the body becomes dark and muddy-looking. Sometimes a general bronzing of the skin takes place. At other times irregular patches of pigmentation appear on various parts of the body. The parts generally affected are the face, neck, the sides of the chest, the nipples, the abdomen, the lumbar region, the axillæ, and the flexures of the arms and thighs. The [illegible] more or less dark brown in [illegible] the skin on the front of the chest. [illegible] sometimes [illegible] eyelids.

[illegible] been noticed occasionally.

The association of scleroderma with Graves' disease has been recorded by several observers.

Mention must also be made here of the occurrence of a fleeting oedema which appears and disappears quickly in various parts of the body. Factitious urticaria has also been observed.

The nutrition of the hair also is generally affected. Many patients complain of the thinness and falling out of the hair, which is abnormally dry as well as scanty. The hair of the eyebrows and eyelids may also fall out. The axillary and pubic hair may similarly be affected. Almost universal alopecia has been recorded.

In connection with the change in the hair, it may be pointed out that the teeth also frequently become carious during the course of the disease.

Anaemia is often present to a certain degree among the younger patients, but is not a constant symptom. That it may be a marked feature of the disease is shown by the fact that Begbie considered it to be the primary factor in the malady, while Wilks has cautioned the inexperienced to beware of mistaking cases of Graves' disease for ordinary anaemia.

Epistaxis is not infrequent in the course of the disease as well as before it; of this we have had a number of examples. Trousseau recorded the occurrence of pulmonary, intestinal, meningeal, and cerebral haemorrhages.

Dr. Dreschfeld has lately called attention to the occurrence of acetonaemia in connection with attacks of persistent vomiting, to which reference will be made farther on.

In the *respiratory system* the chief troubles are [illegible] cough and attacks of dyspnoea. The cough is generally dry, like that observed in cases of ordinary goitre. The attacks of dyspnoea are attended with aggravation of all the symptoms, swelling of the vessels of the neck, [illegible] of the face, and impending asphyxia. Such attacks have at times proved fatal. It has been supposed that they arise from a sudden increase of direct pressure of the goitre on the trachea; and this is [illegible] by the resemblance they bear to the similar attacks which [illegible] on the trachea [illegible] and [illegible] the trachea bears evidence of having been compressed [illegible] con- [illegible] they [illegible]

[illegible]

[illegible] the system. Œdema has been observed to be more marked on one side than on the other; this is independent of position, and is associated with vasomotor disturbances. A very interesting form of swelling has been observed by us in which the lower extremities become greatly enlarged without any pitting. Such non-pitting swelling was first described by [illegible], and is probably of the same nature as the swelling which is observed in myxœdema.

The digestive system is commonly disturbed. The appetite is often capricious, and the patient, like a pregnant woman, has longings for unusual kinds of food. Sometimes the appetite is ravenous, and the patient can hardly wait for the conveyance of the food to the mouth. On the other hand, especially when the disease is progressing unfavourably, there may be more or less complete anorexia. Excessive thirst is also a frequent symptom, and the patient will sometimes gulp down water with the greatest eagerness and impatience. Vomiting, apparently unrelated to the ingestion of food, is not uncommon. Looseness of the bowels is a very frequent symptom. It is apt to come on without apparent cause, and as a rule is attended with no griping. The patient may have four or five loose motions in the course of the day, and this may continue for a week or a fortnight at a time. Sometimes acute attacks of diarrhœa may supervene, which completely prostrate the patient and occasionally prove fatal.

Vomiting sometimes becomes a very grave symptom. The patient complains of epigastric pain, and can retain nothing on the stomach. Dr. Dreschfeld states that in seven cases where such attacks have occurred, he observed that the breath had a peculiar sweet odour, and that the urine not only [illegible] of acetone, but gave the characteristic reaction of diacetic acid. With the vomiting there is intense prostration, restlessness, and the [illegible] of air hunger observed in diabetic coma. Fortunately these symptoms not infrequently pass off, but they occasionally end in death. Sometimes vomiting and diarrhœa occur together.

[illegible] generally [illegible] by Warburton [illegible] feature [illegible] in [illegible] to the occurrence of pregnancy. As has been pointed out, patients frequently improve during pregnancy, and generally go to full time. In some of the cases under our care severe flooding occurred after delivery. As a rule, in them also the influence of pregnancy was favourable; although we have observed cases where the symptoms of the disease have appeared for the first time during gestation.

We now come to what are the most interesting of the symptoms of this complex disease, those, namely, affecting the

Nervous system.—A change in the mental condition of the patient is often one of the earliest symptoms. She becomes abnormally irritable, excitable, fidgety, and restless. She longs for continual change, and feels she must constantly be seeing or doing something new. Often she is quite uncomfortably conscious of this alteration, and will tell the physician all about it; at other times he only hears of it through the patient's friends. At one time she is low-spirited and lachrymose, at another she is buoyant and smiling. The moral nature is often perverted, so that the patient becomes spiteful, untruthful, suspicious, and generally discontented. She is wayward and wilful, and cannot bear to be thwarted or contradicted. She is readily upset by any unusual occurrence. A sudden loud knock at the door, or the arrival of a telegram, may throw her into a state of great agitation, perhaps lasting for hours. She is profoundly affected by the receipt of good or bad news. Such patients are very trying to relations and friends with whom they live, or to the nurses who attend upon them. The sleep is often disturbed; the restless patient tosses about in bed, is troubled with disagreeable dreams, and is apt to wake up in a fright. Sometimes she walks in her sleep or jumps out of bed, and wakes to find herself on the floor.

Although mental changes are common, cases are met with now and then in which the patient remains placid, good-tempered, and generally amiable. In other cases, again, more serious mental changes occur, and the patient becomes quite insane. Melancholia and mania are the usual forms which the insanity assumes. Such cases are usually fatal.

Headache is frequently complained of, but presents no peculiar features. Those affected with the disease are also liable to neuralgias of various kinds.

The tremor or trembling, already mentioned as one of the cardinal symptoms, belongs, of course, to disorders of the nervous system. Among the other nervous symptoms are painful cramps. These often occur in the extremities, especially in the hands and feet; they commonly come on in the feet and legs at night-time. As a rule, these cramps do not last long; but occasionally we have observed more persistent spasm in which the hands assume the characteristic form seen in tetany.

Another trouble which patients experience is giving way of the legs when walking or standing. They feel their knees suddenly giving way, and they either fall or save themselves with difficulty. It is interesting to notice that the same symptom is common in myxœdema.

A decided feebleness in the lower extremities, almost amounting to paraplegia, has been observed in some aggravated cases of the disease. Hemiplegia and monoplegia have also been observed, but these are decidedly rare. The tendon reflexes are present and are generally brisk.

Varieties of the disease; course and duration.—A well-marked case of Graves' disease is very readily recognised at first sight. The malady is typical when all the four cardinal symptoms—goitre, exophthalmos, rapid cardiac action, and trembling—are present. When the chief symptoms are present, many of the others will be found also. Of these chief signs, exophthalmos is that by means of which the nature of the case is usually recognised.

It must be borne in mind, however, that the disease is often incomplete, and in its slighter forms may easily be overlooked. The most important and most essential symptom is the rapid cardiac action. The goitre and the exophthalmos may be present in very varying degree.

The enlargement of the thyroid may be so slight that the patient may never have been conscious of it, and at the time she comes under the observation of the physician none may be perceptible. The exophthalmos may exist to such a small extent as to escape notice.

We hesitate to go so far as Trousseau, who said: "I believe that the disease may be foreseen, and does really exist in a great number of instances without there being exophthalmos, bronchocele or extreme frequency of the pulse." Without at least one of these features with some of the associated symptoms we do not consider the diagnosis of the disease can be made. We are, however, satisfied that incomplete forms of the disease (*formes frustes*) are not at all uncommon. Charcot and Marie have specially called attention to the incomplete forms. Two varieties of the disease may thus be described—the *complete* and the *incomplete*. The manifestation of the complete form of the disease throws light on the incomplete form. In some cases all the four main symptoms appear more or less simultaneously. More commonly, however, one or two symptoms show themselves first. Thus rapid cardiac action with tremor and palpitation and some of the secondary symptoms may first appear, while exophthalmos or goitre, or both, follow later. Indeed the malady may subside without the appearance of the latter, and the case is then an incomplete one. Sometimes exophthalmos is the first symptom to appear, sometimes it is the last. Most commonly the goitre is the first sign of the disease. The incomplete form is characterised by rapid action of the heart, tremor, nervous irritability, together with probably slight swelling of the thyroid and slight ocular symptoms.

Again, the disease may be divided into *the acute* and *the chronic* forms; the latter of common occurrence, the former more rare. In the acute cases the symptoms may disappear within a few days. A number of the reported cases have been in quite young children. In a case reported by Moore the symptoms, which appeared in a young girl on reading a letter telling of her brother's death, lasted only two days. Solbrig has reported a case of a boy aged eight, who, after suffering from palpitation, enlargement of the thyroid, and prominence of the eyes, entirely recovered after twelve days. A case in a girl of ten years, where the duration was six weeks, was reported by Muller; the symptoms were extreme awkwardness in the movements of the hands, frequent vomiting, lassitude, and pains all over the body followed by exophthalmos and swelling of the thyroid.

Numerous cases have been related where the duration has been no more than three or four months.

Besides these cases of short duration followed by recovery, there are others where the illness has ended fatally within six weeks of the onset The acute cases are, on the whole, extremely rare; and it is evident from those which have been recorded that in them recovery is commoner than death.

A considerable number of the chronic cases begin more or less acutely, and in the course of a chronic case acute symptoms may appear, so that no hard and fast distinction can be drawn between the two forms.

Another division may be made into *primary* and *secondary* cases. The secondary cases are those where the disease occurs in a patient who has previously suffered from ordinary goitre; these cases are not very common

While the duration of the acute cases varies from a few days to a few months, that of the chronic cases is, as a rule, to be measured by years. We have had cases under our care where the duration of the disease has been over twenty years.

Relapses are not at all uncommon. Sir R. Gowers speaks of a patient who had three attacks at intervals of several years. Trousseau relates the case of a lady who, for the sixth time during six years, presented all the symptoms of the disease, and each time was much benefited by hydropathic treatment. Dr. Huggard of Davos Platz has shown us the case of a lady who relapsed repeatedly on leaving the high altitudes, and finally presented some of the symptoms of myxœdema. Mobius speaks of relapses as the rule. They may occur after years of apparent recovery. Our opinion is that in these cases the disease has really never subsided; that the recovery has been apparent only, and that the relapses may more properly be considered as exacerbations or recrudescences of the malady. The possibility of relapse must be taken into consideration in making a prognosis.

A *sequel* to exophthalmic goitre which has now been observed in a significant number of cases is myxœdema. Occasionally the two conditions seem to be combined; the symptoms of myxœdema supervening, while those of exophthalmic goitre are still present. Sometimes myxœdema follows closely on exophthalmic goitre, but there may be a long interval between the time of onset of the two diseases.

Death may occur directly from the malady itself or as the result of intercurrent diseases. The end may be sudden and due to syncope Syncope may occur in patients who are apparently going on well. Thus Dr. Hale White mentions the case of a young woman, an in-patient in the

Hospital, but not ill enough to be confined to bed, who, seeing the electric current applied to another patient, asked that it might be tried on herself. On the application of the current she fell back dead, having been laughing and talking only an instant before she died. It is, however, more usual to have some previous evidence that the case is not progressing satisfactorily. A form of marasmus occasionally ensues and the patient becomes greatly emaciated and prostrated. Persistent vomiting, diarrhœa, and dyspnœa may usher in death. In this condition also death may occur from cardiac failure. Sometimes mania occurs and precedes death.

In about half of the fatal cases the end comes from intercurrent diseases. Of the latter the commonest are pneumonia, bronchitis, and cardiac disease. The disease may prove fatal at almost any stage. We have mentioned that death may occur within six weeks of the onset. We have observed a fatal termination in a case of fifteen years' standing.

Diagnosis.—There is no difficulty about the diagnosis when the symptoms of the disease are well marked. Slightly marked cases are frequently overlooked on too cursory an examination. The combination of symptoms which have been described cannot, however, be mistaken for any other disease.

Prognosis.—It will be gathered from the account we have given of the course of the disease that a guarded prognosis must always be given. The duration, the course, and the end of the disease in any individual case must be uncertain. Relapse, as we have seen, occurs even after the apparent subsidence of the disease. The more severe the symptoms the greater will be the anxiety as to the issue. Progressive emaciation, loss of strength, great rapidity of the heart's action, anorexia, continued vomiting, diarrhœa, dyspnœa, muscular tremors, must all be looked on as symptoms of grave omen; on the other hand, many cases present a mild course throughout, and in these a hopeful prognosis may be given with some confidence.

The disease is, as a rule, so long drawn out that many cases get lost sight of, especially in hospital practice; and a good deal of uncertainty thus prevails as to the issue of them.

We have summarised the result in thirty-three patients observed by us in which the disease either lasted over five years or ended fatally. Dr. R. T. Williamson has similarly tabulated the result in twenty-four cases observed at the Manchester Infirmary.

Result in Fifty-seven Cases.

	Our own Series.	Dr. Williamson's Series.	Total.
Fatal termination . .	8	6	14
Recovery complete . .	5	5	10
Recovery almost complete . .	9	2	11
Improvement considerable	9	4	13
Improvement slight . .	1	3	4
In statu quo . . .	1	3	4
Alive, but exact condition not known	0	1	1

Bushan, out of 900 cases collected by him from records, found a fatal result recorded in 105. We think we shall not be far wrong in saying that in about 25 per cent of the well-marked cases death will result from the disease. In about 50 per cent more or less complete recovery will eventually take place.

There does not seem to be any guide to the duration of the malady. Before they disappear the symptoms may last from a few months to many years.

Even when recovery takes place, the disease as a rule does not leave the patient as she was before the attack. Trousseau remarked when recovery took place that swelling and induration of the thyroid with prominence of the eyeballs always remained. In the generality of cases, no doubt, this is true; but sometimes the exophthalmos quite disappears and the goitre may vanish. The latter is more likely to be the result if the exophthalmos be moderate and the goitre small. The longer exophthalmos lasts, and the more extreme it is, the more probable is it that it will be permanent.

It is interesting to note that, according to Dreschfeld, the prognosis of exophthalmic goitre in children is not unfavourable. Some of the little patients recover completely; in others, as in adults, a certain degree of goitre and exophthalmos may remain without other troubles. In the few cases in children which have ended fatally, death has resulted from intermittent affections, and not from the disease itself.

Morbid anatomy.—General emaciation is usually first to be noted. The prominence of the eyes is not so marked after death as during life. An excess of fat in the orbits, or rather an excess as compared with the general amount of fat in the body, has been observed. The thyroid gland shows general and uniform enlargement. The thymus gland is often not only persistent, but large. An increased amount of connective tissue in the neck, enlarged cervical and bronchial glands, and enlargement of the lymphatic structures of the intestines, have sometimes been recorded. The spleen is occasionally enlarged. There are usually no naked-eye changes in the nervous system.

The heart may be normal, dilated, or the seat of valvular disease. The lungs are unaffected save for accidental complications, of which pneumonia is the most common.

The condition of the thyroid and thymus glands must be more particularly considered. It has been alleged that the thyroid gland in this disease is extremely vascular. The vascularity is, however, principally superficial. The veins over the capsule are dilated and numerous The nutrient arteries are also enlarged, tortuous, and dilated. Dr. Greenfield observes that in cases examined by him there has been no increase in vascularity of the gland itself, but rather a diminution. Mr. Edmunds, however, states that a remarkable hypertrophy of the blood-vessels is sometimes found, and F. T. Paul is of opinion that the vascularity of the gland in Graves' disease is decidedly greater than in other forms of goitre. The vascularity of the gland seems to be simply the result and the concomitant of increased activity, and will vary according to the stage of the disease. For this reason it is more likely to be observed in the specimens removed by the surgeon than in those which are obtained in the post-mortem rooms. The enlargement of the gland is a general one. On section the tissue is firm but elastic, and of a brownish colour; its consistence is less than that of the ordinary gland. Sometimes there are irregular swellings due to encapsuled masses of tissue in which are numerous islands of colloid material.

On microscopic examination the striking feature is the great increase of secreting structure. The secreting structure, moreover, is not merely increased, but is much altered. The epithelium lining the vesicles is changed in form from the cubical to the columnar type; there is increased proliferation also, so that the lining membrane becomes convoluted, and papillary projections into the spaces are commonly seen. The secretion contained in the vesicles is more mucous than the ordinary colloid, and stains much less deeply. Desquamation of the epithelium is not uncommon, so that the vesicles contain detached columnar cells. In addition to the changes in the vesicles there is the production of a great number of newly-formed tubular spaces lined by a single layer of cubical epithelium. These columns, as Dr. Greenfield points out, closely resemble the tubules of a secretory gland.

At a later period the gland may become firmer from the growth of fibrous tissue, and the proliferative changes may be obscured.

Edmunds has shown the great similarity between the gland-tissue in exophthalmic goitre and that in an animal which has had a large portion of the thyroid removed by operation. From this he infers that the alteration in the thyroid gland in Graves' disease is of the nature of compensatory hypertrophy.

Greenfield has pointed out the resemblance in appearance of the goitre to a salivary gland. The goitre, according to him, bears the same relation to a normal gland that the mammary gland during lactation bears to the quiescent gland.

The persistence and enlargement of the thymus gland is certainly a very frequent if not a constant feature of the disease. Isolated cases were recorded by Markham and Goodhart many years ago. In all the cases we have recently examined post-mortem at St. Thomas's Hospital we have found this condition, and the experience of pathologists at other hospitals is to the same effect. The thymus gland in these cases consists of two flat triangular fleshy bodies lying behind the manubrium sterni, and reaching down to the pericardium, over the upper part of which they are spread out like an apron. Unless specially looked for, the thymus may be easily missed.

The thymus tissue, under microscopical examination, presents no features different from those of the gland under ordinary circumstances, but shows the usual structure, including the corpuscles of Hassall.

Alterations in the sympathetic have been described by some pathologists, but it has not been shown that the changes found are in any way peculiar to exophthalmic goitre. Dr. Greenfield describes swelling of the ganglia with marked hyperæmia in the more superficial parts, active invasion of the tissue by leucocytes, and degenerative changes in the ganglion cells.

As regards the central nervous system, minute hæmorrhages have been observed by Greenfield and Hale White; but beyond these there is nothing of importance. Most careful and thorough examination of the pons medulla and other parts in a case at St. Thomas's Hospital failed to reveal any microscopical changes.

Pathology.—A great many hypotheses have been propounded to explain the curious symptoms of this disease. It has been ascribed to an altered condition of the blood, to an affection of the sympathetic, to a derangement of the emotional nervous system, to a disorder of the ganglia about the fourth ventricle, and finally to the diseased condition of the thyroid gland itself. We have seen that there are no characteristic changes in the blood, and such as have been observed do not appear to stand in any causative relation to the disease. The sympathetic ganglia, it is true, in some cases, have been found diseased; but this is not a constant feature. Only some of the symptoms of exophthalmic goitre can be explained by affection of the sympathetic, and it is impossible to formulate a satisfactory theory of the malady on this basis. The derangement of the emotional nervous system will explain a good deal, but does not account for the enlargement and over-activity of the thyroid, nor for the persistence and hypertrophy of the thymus.

The same may be said as regards a disorder of the ganglia in the neighbourhood of the fourth ventricle. We think that too much importance has been attached to a few, as yet unconfirmed, experiments by Filehne on animals. He claimed in one case to have produced exophthalmos, enlargement of the thyroid, and increased cardiac action, by dividing the anterior fourths of the restiform bodies. Minute hæmorrhages in the medulla are found in a variety of affections besides exophthalmic goitre—in myxœdema, for example—and are clearly the result, not the cause of the disease. No mere limited lesion of the bulbar nuclei could explain the widely spread character of the symptoms.

Since a knowledge has been gained of the great functional importance of the thyroid gland, exophthalmic goitre has been attributed by many writers to a disease of this organ. Mobius was one of the earliest of those who supported this opinion.

We have seen that the gland has a much increased blood-supply, and that the microscopical appearances show increased secretory activity with hyperplasia of the epithelium. It may with reason be inferred from this that an amount of thyroid secretion greater than usual will be discharged into the circulation. If the change in the thyroid be the cause of all the symptoms of the disease we should expect to find in it the reverse of the picture in myxœdema. The contrast which the two diseases present has been dwelt on by many writers, and especially by Möbius. Comparing the myxœdema patient on the one side with the victim of exophthalmic goitre on the other, we see many points of contrast. One patient, the myxœdematous, gets more and more bulky, while the other steadily loses flesh. The one is intolerant of cold, the other of heat. The skin of the one is dry and swollen, of the other moist and shrunken.

The temperature of the one rarely rises above the normal; that of the other rarely if ever falls below it. The one is slow, placid, and deliberate; the other quick, irritable, and impulsive. The heart's action in the one is quiet, in the other rapid.

We know that the secretion of the thyroid gland when administered to a patient in large doses, either by subcutaneous injection or by the mouth, has the power of increasing the rate of the heart's action, of causing loss of body-weight, and of stimulating the action of the skin. It raises the subnormal temperature of the myxœdematous patient to the normal or above it, and in over-doses produces vomiting, headache, and violent pains in the limbs. If over-activity or over-secretion of a hypertrophied thyroid gland were the whole disease, it ought to be possible to produce it by the administration of large quantities of thyroid gland. No one has yet succeeded in causing exophthalmos in this way.

It is here that the hypothesis that the disease is due to over-action of the thyroid gland fails. The supporters of this hypothesis have, therefore, fallen back on another surmise; namely, that not merely is the gland over-active, but that its secretion, besides being increased, is also perverted. Of this we have at present no absolute proof.

Some have supposed that the primary disease may be in the parathyroids. The resemblance of many of the symptoms of exophthalmic goitre to those of athyroidea, which there is good reason to believe depends on removal of the parathyroids, has been pointed out by Edmunds and others. Exophthalmos, however, has not been observed to follow removal of the parathyroids during the short time which the animals survive this operation.

No explanation has yet been given of the relation of the persistent thymus to the disease.

Treatment.—The natural course of the disease is so variable that there is great difficulty in correctly interpreting the effects of treatment. Under similar conditions as to treatment some cases improve rapidly, some remain stationary for a long time; others fluctuate, or steadily lose ground, and end fatally. It is not surprising that a great many remedies have been employed for such a disease, and that there should be much difference of opinion as to their value. Hygienic measures are of great importance. The diet should be carefully regulated. It will be found that the patient has sometimes a craving for most unsuitable articles of food, such as nuts, pickles, shell-fish, pastry, and ices. Such things should be strictly prohibited. Meals should be taken at regular intervals, and should consist of plain, wholesome, well-cooked meat, with a proper proportion of vegetables and fruit. In regard to the amount of the latter we must be guided by the condition of the bowels. Tea and coffee should be allowed with discretion, and in small quantity. The patient, as a rule, is better without alcohol. The disease being so rare in men, it is almost superfluous to say that tobacco should be forbidden in all its forms.

In the less severe forms of the disease a moderate amount of exercise in the open air is beneficial. Dancing, sight-seeing, visiting theatres and picture galleries, and shopping should be prohibited. If the patient be sent away to some health resort, special injunctions in regard to this matter should be laid down; as the benefits of the change of air and scene may be altogether counterbalanced by the excitement of social entertainments.

In severe cases, where the heart's action is very rapid and the patient is losing ground, rest in the recumbent position should be ordered.

Change of air and change of scene often prove most beneficial. The change should be as thorough and as restful as possible. Sometimes the seaside suits the patient better, sometimes an inland health resort. Mountain air, especially the high altitudes of Switzerland in winter, has occasionally proved of great service. A sea-voyage also has been credited with an occasional cure.

Baths of many kinds have been found useful; but it is difficult to see how they act in the case. Tepid sea-water baths or effervescing mineral baths have been found serviceable; but open sea-baths, cold and hot baths should be avoided. Hydropathic treatment, douching, and massage are held in much esteem in France for the relief of this malady.

Local cold applications to the thyroid have sometimes been found to quiet the circulation. Leiter's tubes may be conveniently used for this purpose.

The principal drugs which have been employed are those which have an effect on the heart or circulation, on the nervous system, or on the thyroid gland. Thus digitalis and strophanthus have been employed for their action on the heart; belladonna, bromide of potassium, and opium for their effect on the nervous system; while the iodides have been used on account of their influence on goitres in general. As regards digitalis and strophanthus, we have found some patients very intolerant of them; others have derived benefit. A more generally useful drug is belladonna in doses of ten to fifteen minims of the tincture three times a day. Its principal effect appears to be on the nervous system, the patient feeling better and less excitable and restless while taking it; it has, however, little effect on the circulation. Bromide of potassium we have also found useful where the nervous symptoms predominate. It may be given either in combination with belladonna or in a single dose of twenty or thirty grains at bedtime. Opium, which has been recommended by Cheadle and others, is in our experience not well borne. Iodides, except in combination, appear in many cases to aggravate the malady, although in rare cases they may be of benefit. Iron is useful when the disease is combined with chlorosis or a marked degree of anæmia, otherwise it is not beneficial. Arsenic is sometimes of use, and two to five minims of the liquor arsenicalis may be given after meals. A remedy which has lately been much used is phosphate of soda, of which fifteen to thirty grains may be given three times a day. We have used it, but are not convinced that it is beneficial. The glycero-phosphate is said to be better than the ordinary phosphate. Cod-liver oil, if the patient can take it, is useful when there is malnutrition. Some recommend it in large doses, and by the rectum as well as by the mouth. We have given pancreatic emulsion, as recommended by Dr. Dreschfeld, with apparent benefit.

It is unnecessary to add, as regards drugs, that cases must always be treated on general principles. If dyspepsia be present, or diarrhœa, or constipation, the appropriate remedies must be employed. Complications must be treated as they arise. In the attacks of vomiting the patient must be fed by the rectum. Dreschfeld speaks of citrate of potash in large doses as a most useful remedy in checking the vomiting.

Galvanism has been employed for many years. It was first introduced to influence the sympathetic in the neck, one pole being placed at the back of the neck and the other over the sympathetic, first on the one side, then on the other. Weak currents should be used, and the direction may be reversed. The poles may be applied also to the eyes, the thyroid, and the region of the heart.

Vigouroux recommends faradisation in preference to galvanism. The positive pole of a large electrode is applied to the neck, while the negative, a small electrode, is applied in succession to the carotids, to the eyelids, and to the goitre.

We have made a fair trial of both methods, and are very doubtful whether any benefit has followed their use apart from the mental impression made upon the patient.

Of recent years thyroid, thymus, and other organic preparations have been employed. Thyroid gland preparations, theoretically speaking, should always make the disease worse. Although usually we have found the patient's symptoms distinctly aggravated even by small doses, yet we have given large doses without affecting the patient in any way. We have not observed any case where the patient was decidedly benefited. A number of cases of reported benefit from thymus gland preparations having been reported by various observers, we made an extensive trial of them in twenty cases of the disease. The conclusion we came to was that no appreciable effect followed their administration, although in a few cases the patients felt better while taking them.

Trousseau has recorded that great relief has been afforded during attacks of dyspnœa by leeching or bleeding.

Operative treatment has recently been in vogue, principally in Germany. Lister in 1877 removed the bulk of a goitre in a case of this disease where life was threatened by suffocation. In a few weeks all the symptoms were alleviated, and the patient, who was still alive in 1887, then presented few signs of her former malady. Since that time larger or smaller portions of the goitre have been surgically removed in many cases. The most complete statistics on the subject have been published by Starr. Out of 190 cases operated on, 23 died as the immediate result of the operation; 3 were in no way improved; 45 were improved, and 74 were reported as entirely cured: in 45 the results were doubtful. If we compare these results with those of other methods of treatment, we find no striking difference except a death-rate of 12 per cent due to the operation. We have seen that recovery takes place in about 40 per cent, and operation does not give a larger proportion. The risk of death from the operation is much greater in the acute cases than in the chronic, and we consider that operative removal of a portion of the thyroid is never justifiable in an acute case. In a chronic case we should only be disposed to recommend it where the tumour seriously interferes with the breathing, or where other methods of treatment have failed. We have had a portion of the thyroid removed by the surgeon in two chronic cases; in one, where the exophthalmos was extreme, there was no improvement, while in another, where the exophthalmos was slight, decided improvement followed.

The methods of operation have been various. The thyroid arteries have been ligatured, with the object of causing the gland to atrophy The isthmus of the gland has been divided. One lobe, or a portion of one lobe, has been removed. In cases of well-defined adenoma, or cyst, the growth has been enucleated.

A method called exothyropexy, which consists in stripping the capsule from the gland, and so fixing the latter in the superficial wound as to produce shrinkage from exposure to the air and from thrombosis of the venous sinuses, has been introduced by Jaboulay, who has had fourteen successful cases with no death.

Another method of surgical treatment of the disease has recently been carried out by Jaboulay. This consists in section of the cervical sympathetic. Mr. Walter Edmunds suggested the possible utility of this operation as the result of experiments on animals. He found that the proptosis produced in monkeys by subcutaneous injection of cocaine could be lessened by section of the sympathetic. He recommended division of the sympathetic for cases where the prominence of the eyes was so great as to cause ulceration of the cornea. Jaboulay, however, alleges that an actual and lasting cure may be brought about by this operation, which, he says, is easy, and free from ill-effects, immediate or remote. He has operated in six cases, and in all with benefit.

W. M. Ord.
Hector Mackenzie.

REFERENCES

1. Abram, J. H. "Exophthalmic Goitre," *Lancet*, 1895, ii. 1221.—2. Amitrano, A. "Contributo clinico alla patogenesi del morbo di Flajani," *Arch. internaz. d. spec. med.-chir.* Napoli, 1895, xi. 376-81.—3. Augiéras. "Un cas de goitre exophtalmique," *Revue gén. d'opht.* Paris, 1895, xiv. 97-99.—4. Baldwin, W. W. "Some Cases of Graves' Disease succeeded by Thyroid Atrophy," *Lancet*, 18[illegible], i. 145.—5. Barella, Wilhelm. *Ueber einseitigen Exophthalmus bei Morbus Basedowii*, Berl. 1894, G. Schade, 32 pp.

—6. Basedow. *Wochnschr. f. d. ges. Heilk.* Nos. 13, 14, 1840, and Casper's *Wochnschr.* No. 49, 1848.—7. Béclère, A. "Un nouveau cas de myxœdème guéri par l'alimentation thyroidienne ; le thyroidisme dans ses rapports avec la maladie de Basedow et avec l'hystérie," *Bull. et mém. soc. méd. des hôp. de Paris*, 1894, 3 sér. xi. 631-46, 1 plate.—8. Begbie, J. *Edin. Med. Journ.* Feb. 1849.—9. Begbie, Warburton. *Edin. Med. Journ.* Sept. 1863.—10. Berger, E. "Du larmoiement dans le goitre exophtalmique," *Bull. méd.* Par. 1893, vii. 241.—11. Bershing, H. T. "A Case of Exophthalmic Goitre," *Denver Med. Times*, 1891-92, xi. 429-36.—12. Bienfait, A. "Étude sur la pathogénie de la maladie de Basedow," *Ann. soc. med.-chir. de Liege*, 1895, xxxiv. 111-26 ; *Gaz. méd. de Liège*, 1894-5, vii. 328.—13. Boeteau, L. *Des troubles psychiques dans le goitre exophtalmique*, Paris, 1892, G. Steinheil, 114 pp.—14. Bogroff, A. ["Contribution à l'étude de la valeur physiologique de la glande thyroide et de son rôle dans la pathologie et dans la thérapie de la maladie de Basedow"] *Yuzhno-russk. méd. gaz.* Odessa, 1894, iii. 93, 107, 125.—15. Boinet and Bourdillon. "Quelques phénomènes peu communs dans le goitre exophtalmique," *Marseille méd.* 1891, xxviii. 606-609.—16. Boinet, E. and Silbert. "Des ptomaines urinaires dans le goitre exophtalmique," *Rev. méd.* Paris, 1892, xii. 33-47 ; *Marseille méd.* 1892, xxix. 348-67.—17. *Idem.* "Des ptomaines urinaires dans le goitre exophtalmique," *Ann. de l'École . . . de méd. et pharm de Marseille*, 1892, Paris, 1893, 71-90.—18. Bonne, C. "Examen par la méthode de Golgi des nerfs intrathyroidiens dans un cas de goitre exophtalmique," *Revue neurol* Paris, 1895, iii. 521-24.—19. Booth, J. A. "Exophthalmic Goitre ; Thyroidectomy," *New York Med. Journ.* 1894, lix. 375 ; *Boston Med. and Surg. Journ.* 1894, cxxx. 391.—20. *Idem.* "A brief Review of the Thyroid Theory in Graves' Disease ; Report of two Cases treated by Thyroidectomy," *Journ. Nervous and Mental Disease*, N.Y. 1894, xxi. 486-93.—21. *Idem.* "Œdema in Graves' Disease ; Report of a Case of Œdema of the Eyelids ; Thyroidectomy," *Med. Rec.* N.Y. 1896, i. 45.—22. Bottini, E. "L'esterpazione del gozzo nel morbo di Basedow," *Gaz. d. osp.* Milano, 1893, xiv. 97-104.—23 Bouchaud. "Goitre exophtalmique et tremblement héréditaire," *Journ. de sci. méd. de Lille*, 1895, ii. 569-80.—24. Bradshaw, T. R. "Case of Graves' Disease complicated by Hemiplegia and Unilateral Chorea," *Brit. Med. Journ.* Lond. 1891, i. 1384.—25. Bramwell, B. "Exophthalmic Goitre," *Atlas of Clinical Medicine*, fol. Edinb 1892-93 ; ii. 91-103, 2 plates.—26. Brandenburg, G. *Die Basedow'sche Krankheit.* Leipzig, 1894, B. Konegen, 136 pp.—27. Le Breton and Vaquez. "Un cas de myxœdème infantile ; traitement thyroidien ; modifications du sang," *Bull. et mém. soc. méd. des hôp. de Paris*, 1895, xii. 22-29.—28. Briddon, C. K. "Exophthalmic Goitre," *Annals of Surgery*, 1895, xxi. 66—29. Briner, O. "Ueber die operative Behandlung des Basedow'schen Krankheit durch Strumektomie," *Beitrage zur klin. Chirurgie*, Tubingen, 1891, xii. 704-750.—30. Brissaud, E "Les lésions thyroidiennes et la théorie nerveuse de la maladie de Basedow," *Archives clin. de Bordeaux*, 1895, iv. 289-318.—31. *Idem* "Cuerpo tiróides y enfermedad de Basedow," Transl. *Semana méd.* Buenos Aires, 1895, ii. 329, 335.—32. *Idem.* "Sur un cas de mort par exothyropexie pour un goitre exophtalmique," *Méd. mod.* Paris, 1894, v. 243-45.—33. *Idem.* "Corps thyroide et maladie de Basedow [rapport]," *Ann. de méd. scient. et prat.* Paris, 1895, v. 281-87 ; *Courier méd.* Paris, 1895, xlv. 266, 273 ; *Semaine méd.* Paris, 1895, xv. 326-30 ; *Archives de neurol.* Paris, 1895, xxx. 225-42 ; *Bull. méd.* Paris, 1895, ix. 743-54 ; *Journ. de Conn. méd. prat.* Paris, 1895, 294, 302, 309 ; *Presse méd Belge*, Brux. 1895, xlvii 280-83.—34. Bruhl, I. "Des rapports du goitre simple avec la maladie de Basedow ; des faux goitres exophtalmiques," *Gaz. d. hôp.* Paris, 1891, lxiv. 683, 701.—35. Bruns, L. "Ueber das Grafe'sche Symptom bei Morbus Basedowii," *Neurol. Centralbl.* Leipz. 1892, xi. 6-13.—36. Bryson, Louise F. "Exophthalmic Goitre," *Post-Graduate*, N.Y. 1891-2, vii. 269-274.—37. Burr, C. W. "Exophthalmic Goitre," *Philad. Polyclin.* 1893, ii. 46-50.—38. Buschan, G. *Die Basedow'sche Krankheit*, 1894.—39. *Idem.* *Die Basedow'sche Krankheit* (*Goitre exophtalmique, Graves' Disease, morbo di Flajani*), *eine Monographie*, Leipz. u. Wien, 1894, F. Denticke, 184 pp.—40. Cardew, H. W. D. "The Electrical Treatment of Graves' Disease," *Abstr. Trans. Hunterian Soc.* Lond. 1892-93, 62-66.—41. *Idem.* "The Value of diminished Electrical Resistance of the Human Body, as a Symptom in Graves' Disease," *Lancet*, 1891, i. 483-485.—42. *Idem.* "The Practical Electro-Therapeutics of Graves' Disease," *Lancet*, 1891, ii. 6, 64.—43. Chamberlain, Frederick. *Contribution à l'étude de la maladie de Basedow et en particulier de sa pathogénie*, Paris, 1894, 211 pp. No. 208.—44. Charcot, J. M. "Les formes frustes," *Gaz. des hôp.* 1885 and 1889.—45. Chéron, P. "Étiologie, pathogénie et traitement du goitre exophtalmique," *Tribune méd.* Paris, 1895, 2 sér. xxvii. 931-36.—46. *Idem.* "Traitement du goitre exophtalmique," *Union méd.* Paris, 1896, 4 s. ii. 301-313.—47. Chibret. "Le salycilate de soude dans la goitre exophtalmique," *Revue gén. d'ophtalmologie*, Paris, 1895, xiv. 1-3.—48. Chvostek, F. "Ueber alimentare Glykosurie bei Morbus Basedowii," *Wien. klin. Wochenschr.* 1892, v. 251, 267, 325.—49. Colquhoun, D. "Graves' Disease," *New Zealand Med. Journ.* Dunedin, 1894, vii. 144-56.—50. Corbin, T. W. "On Myxœdema," *Australas. M. Gaz.* Sydney, 1894, xiii. 155.—51. Cordell, E. F. "Some Remarks on Exophthalmic Goitre," *Maryland Med. Journ.* Balt. 1895-96, xiii. 287-90.—52. Craig, J. "An unusual Case of Exophthalmic Goitre," *Lancet*, 1894, i. 1375.—53. *Idem.* "An unusual Case of Graves' Disease," *Dublin Journ. Med. Sci.* 1894, xcvii. 508-516.—54. Crook, J. K. "A Clinical Lecture on Exophthalmic Goitre (Graves' or Basedow's Disease)," *New York Med. Journ.* 1894, lix. 422-24.—55. Curtis, B. F. "Thyroidectomy for Exophthalmic Goitre," *Internat. Clinics*, Philad. 4th ser. ii. 213-16.—56. Davies, A. T. "A case of Myxœdema after Thyroid Treatment," *Trans. Clin. Soc. Lond.* 1893-94, xxvii. 275.—57. Demme, R. "Basedow'sche Krankheit nach Scharlach," *Klin. Mitth. a. d. Geb. d. Kinderheilk. d. Jenner'sch Kindersp. in Bern*, 1819, 81-83.—58. Ditisheim, Max. *Ueber Morbus Basedowii*, Basel, 1895, pp. 92, 3 ch.—59. Dock, G. "Goitre in Michigan," *Med. News*, Philad. 1895, lxvii. 60-63; *Trans. Assoc. Amer. Phys.* Philad. 1895, x. 101-107.—60. Doléris, G. A. "Affections génitales de la femme et la maladie de Basedow," *Bull. et mém. soc. obst. et gynéc. de Paris*, 1895, 298-314; *Journ. de méd. de Paris*, 1895, 2 sér. vii. 465, 491; *N. archives d'obst. et de gynéc.* Paris, x. 241-254.—61. O'Donovan, C. "A Case of Exophthalmic Goitre treated during two Years with Tincture of Strophanthus," *Maryland Med. Jour.* Balt. 1894-95, xxxii. 208-210.—62. Daugherty, C. A. "Exophthalmic Goitre, with a Report of Cases," *Trans. Indiana Med. Soc.* Indianop. 1895, xlvi. 168-78 —63. Dreesmann, H. "Die chirurgische Behandlung des Morbus Basedowii," *Deutsche med. Wochnschr.* Leipzig, 1892, xviii. 90-93.—64. Dreschfeld, J. "Notes on Graves' Disease," *Practitioner*, Lond. 1896, lvii 135-154.—65. Drummond, D. *Brit. Med. Journ.* May 1887.—66. Durduff, G. N. "Pathogenesis of Basedow's Disease," *Bolnitsch. gaz. Botkina*, St. Petersb. 1893, iv. 71, 101.—67. Edgeworth, F. H. "Notes on a Case of Exophthalmic Goitre," *Bristol Med.-Chir. J.* 1896, xix. 41-47.—68. Edmunds, W. "Pathology of Graves' Disease," *Journ. Path. and Bacteriol.* Lond. Jan. 1896; *Trans. Path. Soc. Lond.* vols. xlvi. and xlvii.—69. *Idem.* "Observations and Experiments on the Pathology of Graves' Disease," *Journ of Pathol. and Bacteriol.* Edinb. and Lond. 1894-96, iii. 488-501, 11 plates.—70. Ehrlich, Hans. *Ueber Morbus Basedowii im kindlichen Alter*, Berl. 1890, G. Schade, 31 pp.—71. Eshner, A. A. "A Case of Exophthalmic Goitre," *Philad. Polyclinic*, 1895, iv. 285.—72. Eulenburg, A *Ziemssen's Handb.* 1875.—73. *Idem.* "Ueber Astasie-Abasie bei Basedow'scher Krankheit," *Neurol. Centralbl.* Leipzig, 1890, ix. 706-710.—74. *Idem.* "Basedow'sche Krankheit und Schilddruse," *Deutsche med. Wochenschr.* Leipzig u Berl. 1894, xx. 769-72.—75. Ewald, C. A. "Ueber einen durch die Schilddrusentherapie geheilter Fall von Myxodem nebst Erfahrungen über anderweitige Anwendung von Thyreoideapraparaten," *Berl. klin. Wochenschr.* 1895, xxxii. 25, 55.—76. Farner, E. "Beitrage zur pathologischen Anatomie des Morbus Basedowii mit besonderer Berucksichtigung der Struma," *Archiv fur path. Anat.* Berl. 1896, cxliii. 509-74, 1 plate.—77 Ferguson, E. D. "Recent Experience in the Treatment of Exophthalmic Goitre," *Trans. New York Med. Ass.* 1890, vii. 223-230.—78 *Idem.* "Recent Experience in the Treatment of Exophthalmic Goitre," *Gaillard's M. J.* N.Y. 1890, li. 511-516.—79 *Idem.* "An Additional Note on the Use of Strophanthus in the Treatment of Exophthalmic Goitre," *Journ. Amer. Med. Assoc.* Chicago, 1893, xxi. 187-189.—80 Ferri, L. "Delle cause del sintomo di Grafe nel morbo di Basedow," *Gior. d. r. accad. di med. di Torino*, 1892, 3 s xl. 172-180.—81. Flajani, G. *Collez. d' osserv. e rifless. di chirurg.* Rome, 1802.—82. Foot, A. W. "Graves' Disease," *Internat. Clin* Philad. 1892, 2nd s. i. 57-75.—83. Forster, R. "Ein Fall von Braunfarbung der Haut nach langerem Arsengebrauch bei Basedow'scher Krankheit," *Berl. klin. Wochnsch* 1890, xxvii. 1150-1152.—84. Freiberg, A. H. "The Surgical Treatment of Exophthalmic Goitre," *Med. News*, Phila. 1893, lxiii. 225-230.—85. Fridenberg, P. "A Case of Exophthalmic Goitre, with Monocular Symptoms and Unilateral Thyroid Hypertrophy," *Med. Record*, N.Y. 1895, xlviii. 46-49.—86. *Idem.* "Ueber einen Fall von Graves'scher Krankheit mit Exophthalmus monocularis und einseitiger Schilddrüsen Anschwellung," *Archiv für Ophthalmologie*, Leipzig, 1895, xli. 3 Abth. 158-68, 1 plate.—87. Fürst, A. "Bemerkungen zum Morbus Basedowii," *Deutsche* *med. Wochenschr.* Leipzig u. Berl. 1895, xxi. 338.—88. GARAMPAZZI, C. "Due casi di maschera nel morbi di Flajani," *Gazz. d. osp.* Milano, 1890, xi. 530-533.—89. GAUTHIER, G. "Corps thyroide et maladie de Basedow," *Lyon méd.* 1895, lxxx. 5-12 —90. GERHARDT, C. "Ueber krankhafte Pulsationen bei Schlussunfahigheit der Aortenklappen und bei Basedow'scher Krankheit," *Charité-Annalen*, Berlin, 1893, xviii. 243-48.—91. *Idem.* "Ueber das Verhalten der Korperarterien bei Basedow'scher Krankheit," *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* Jena, 1896, i. 135-138.—92. VON GERNET, R. "Ein Beitrag zur Behandlung des Myxodems," *Deutsche Zeitschr. f. Chir.* Leipzig, 1894, xxxix. 455-66.—93. GIOVANELLI, G "Contributo alla sintomatologia e cura del morbo di Basedow," *Gazz. med. di Pavia*, 1893, ii. 289, 313, 337, 366.—94. GLAX. "Zur Klimatotherapie des Morbus Basedowii," *Internat. klin. Rundschau*, Wien, 1894, 1505-7 ; *Wiener med. Presse*, 1894, xxxv. 1878.—95. "Goitre (le) exophtalmique d'après les traveaux récents ; pathogénie et symptômes," *Union méd.* Par. 1896, 4 s. ii. 229-234.—96. "Graves' or Basedow's Disease in Animals," *Lancet*, 1892, ii. 427.—97. GRAWITZ, E. "Morbus Basedowii ; its Symptomatology," *Internat. Clinics*, Philad. 4th ser. iv. 85-93, 1 plate.—98. GREENFIELD, W. S. "On some Diseases of the Thyroid Gland," *Brit. Med. Journ.* vol ii. 1893.—99. GREIDENBERG, B. S. "On Mental Alienation in Basedow's Disease," *Vestnik. Klin. i sudebnoi psichiat. i nevropatol.* St. Petersb. 1893, x. pt. 1, 183-194.—100. GROHMANN, MAX. *Beitrage zur Aetiologie und Symptomatologie des Morbus Basedowii*, Berl. 1894, G. Schade, 31 pp.—101. GRUBE, K. "Zur Aetiologie der Basedow'schen Krankheit," *Neurologisches Centralblatt*, Leipzig, 1894, xiii. 179-83.—102. GUTTMANN, P. "Das arterielle Strumagerausch bei Basedow'scher Krankheit und seine diagnostiche Bedeutung," *Deutsche med Wochnschr.* Leipzig u. Berl. 1893, xix. 254.—103. HALL, A. G. "A Clinical Lecture on Exophthalmic Goitre," *Clin Journ.* London, 1895-96, vii. 38-40.—104. HAWTHORN, C. O. "A Case of Graves' in a Patient the Subject of Articular Rheumatism and Mitral Stenosis," *Glasgow Med. Journ.* 1895, xliii. 446.—105. HAY, C. M. "Exophthalmic Goitre with Mental Disease ; Report of Three Cases with Rare Complications," *Med. Age*, Detroit, 1891, ix. 327-334.—106. HEKTOEN, L. "Hyperplastic Persistent Thymus in Exophthalmic Goitre," *Internat. Med. Mag.* Philad. 1895-96, iv. 584, 594.—107. HERRICK, J. B. "Exophthalmic Goitre," *Internat. Clin.* Philad. 1894, 4th ser. ii 32-36.—108. HERSKIND, E. "Om den kirurgiske Behandling og Patogenesen af Mb. Basedowii," *Biblioth. f. Laeger*, Kjobenh. 1894, 7 R. v. 204-42.—109 HEZEL, O. "Ein Beitrag zur pathologischen Anatomie des Morbus Basedowii," *Deutsche Ztschr. f Nervenh.* Leipzig, 1893-94, iv. 353-358.—110. HIRSCHBERG, L. "Ueber die Basedow'sche Krankheit ; historisch-kritische Studie," *Wiener Klinik*, 1894, xx. Heft 2-3, 15-90.—111. HITSCHMANN, R. "Beitrag zur Casuistik des Morbus Basedowii," *Wiener klin. Wochenschr.* 1894, vii. 923, 945.—112. VAN'T HOFF, L. "Morbus Basedowii ; een pathologische schrickreactie," *Nederl. Tydschr. v. Geneesk.* Amst. 1895, 2 R. xxxi. pt 1, 713-31.—113. HOMÉN, E. A. "Beitrage zur Symptomatologie des Morbus Basedowii," *Neurol. Centralbl.* Leipz. 1892, xl. 427-434. —114. HUCHARD. "Les crises d'amaigrissement dans le goitre exophtalmique," *Rev. prat. d. trav. d. méd.* Par. 1896, liii. 107.—115. ISAAC, RUDOLF. *Beitrag zur Pathologie der Basedow'schen Krankheit.* Siegburg, 1891, W. Reckinger, 35 pp.—116. JABOULAY. "Le traitement du goitre exophtalmique par l'exothyropexie," *Méd. mod.* Paris, 1894, v. 275.—117. *Idem.* "La régénération du goitre extirpe dans la maladie de Basedow et la section du sympathique cervical dans cette maladie," *Lyon méd.* 1896, lxxxi. 389.—118. *Idem. Lyon méd.* March and May 1896 and Feb. 1897.—119. JACCOUD. "Étiologie et traitement du goitre exophtalmique," *Gaz. d. hôp. de Toulouse*, 1890, iv. 377, 385.—120. *Idem.* "Étiologie, pronostic et traitement du goitre exophtalmique," *Gaz. d. hôp.* Par. 1890, lxiii. 1229.—121. JEAFFRESON, C. S. "Thyroid Secretion as a factor in Exophthalmic Goitre," *Lancet*, 1893, ii. 1281.—122. JEANSELME, E. "Sur la coexistence du goitre exophtalmique et de la sclérodermie," *Mercredi méd.* Paris, 1895, vi. 1.—123. JESSNER. "Morbus Basedow ; exitus letalis unter Erscheinungen von Erbrechen, Durchfall, Storing der Hirnfunktionen," *Deutsche med. Ztg.* Berl. 1893, xiv. 804.—124. JESSOP. "Three Cases of Exophthalmic Goitre with Severe Ocular Lesions," *Brit. Med. Journ.* 1895, ii. 1296.—125. JOFFROY, A. "Traitement du goitre exophtalmique," *Union méd.* Par. 1892, 3 s. liii. 649, 673.—126. *Idem.* "Nature et traitement du goitre exophtalmique," *Progres méd.* Paris, 1893, 2 sér. xviii. 477-80 ; 1894, 2 sér. xix. 61, 165, 205, 217.—127. JOFFROY, A., and C. ACHARD. "Contribution à l'anatomie pathologique de la maladie de Basedow," *Arch. de méd. expér. et d'anat. path.* Paris, 1893, v. 807-825. —128. *Idem.* "Maladie de

Basedow et tabes ; observation avec autopsie," *Arch. de méd. expér. et d'anat. path.* Par. 1893, v. 404-409.—129. JOHNSON, F. S. "Exophthalmic Goitre," *Trans. Illinois Med. Soc.* Chicago, 1893, xliii. 193-211.—130. JOHNSTON, G. F. "Clinical Remarks on Exophthalmic Goitre, with Special Reference to its possible Etiology," *Lancet*, 1893, ii. 1121-1123.—131. JOUIN. "Pathologie utérine et maladie de Basedow," *Bull. et mém. soc. obst. et gynéc. de Paris*, 1895, 188-203.—132. JOUSSET, M. "Corps thyroide et maladie de Basedow," *Art. méd.* Paris, 1895, lxxxi. 183-93.—133. KINNICUTT, F. "The Theory of the Origin of Graves' Disease ; with its Bearing on the Surgical Treatment of the Disease," *Med. Rec.* N.Y. 1896, xlix 541-546.—134. KLEINWACHTER, L. "Das Verhalten der Genitalien bei Morbus Basedowii," *Centralbl. f. Gynak.* Leipz. 1892, xvi. 181-185.—135. KRONTHAL, P. "Morbus Basedowii bei einem [illegible] Madchen und dessen Mutter," *Berl. klin. Wochenschr.* 1893, xxx. [illegible] LASVÈNES, GEORGES. *De la maladie de Basedow développée sur un goitre ancien*, Par. 1891, 39 pp. No. 202.—137. LEICHTENSTERN, O. "Ueber Myxodem und uber Einfettungscuren mit Schilddrusenfutterung," *Deutsche med. Wochenschr.* Leipz. u. Berl. 1894, xx. 932.—138. LEMKE, F. "Was wir von der chirurgischen Behandlung des Morbus Basedowii zu erwarten haben," *Deutsche med. Wochnschr* Leipz. u. Berl. 1894, xx. 809-811. — 139. *Idem.* "Ueber chirurgische Behandlung des Morbus Basedowii," *Deutsche med. Wochnschr.* Leipz. 1891, xvii. 47.—140. *Idem.* "Weiteres uber die chirurgische Behandlung des Morbus Basedowii," *Deutsche med. Wochnschr.* Leipz. 1892, xviii. 230.—141. *Idem.* "Ueber Fruhdiagnose und Theorie des Morbus Basedowii," *Munchen. med. Wochnschr.* 1896, xliii. 334-336.—142. LENDON, A A. "Myxœdema and Sporadic Cretinism," *Australas. Med. Gaz.* Sydney, 1894, xiii. 152-55.—143 LEONHARDT, J. S. "Case of Exophthalmic Goitre in the Male," *Memphis M. Month* 1893, xiii. 301-305.—144. LIEBRECHT. "Bemerkenswerthe Falle von Basedow'scher Krankheit aus der Prof Scholer'schen Klinik," *Klin. Monatsbl. f. Augenh.* Stuttg. 1890, xxviii. 492-500.—145. LIÉNAUX. "Deux cas de goitre aberrants chez le chien," *Ann. de méd. vét.* Brux. 355-60.—146 MCADAM, R. L. "A Case of Post-influenzal Graves' Disease," *Australasian Med. Journ.* Melbourne, 1893, n.s. xv. 619-629.—147. MCKEE, J. H. "A Case of Exophthalmic Goitre in a Child," *Philad. Polyclin.* 1895, iv. 33.—148. MACKENZIE, HECTOR. "Clinical Lect. on Graves' Disease," *Lancet*, London, vol. ii. 1890, pp. 545 and 601.—149. *Idem.* "On Œdema in Graves' Disease," *Edin. Med. Journ.* 1897, n.s. vol. i. pp. 401-410. — 150. *Idem.* "Treatment of Graves' Disease," *Amer. Journ. Med. Sci.* Phila. 1897, vol. cxiii. p. 132.—151. MADER. "Morbus Basedowii ; vorubergehende Besserung," *Ber. d. k k. Krankenanst. Rudolph-Stiftung in Wien* (1889), 1890, 270-272 "Basedow'sche Krankheit ; Besserung," *Ber. d. k k. Krankenanst. Rudolph-Stiftung in Wien* (1890), 1891, 300 —152. MANNHEIM, P. *Der Morbus Gravesii (sogenannter Morbus Basedowii).* Berl. 1894, A. Hirschwald, 162 pp. 2 plates.—153. MARCUS. "Das Wesen und die Behandlung der Basedow'schen Krankheit," *Veroffentl. d. Hufeland Gesellsch. in Berl. balneol Gesellsch.* 1893, 187-206.—154. *Idem.* "Das Wesen und die Behandlung der Basedow'schen Krankheit," *Wien. med. Wochnschr.* 1893, xliii. 825, 871, 918, 961.—155. *Idem* "Das Wesen und die Behandlung der Basedow'schen Krankheit," *Deutsche med. Ztg* Berl. 1893, xiv. 529, 541.—156. MARIE, P. "Sur la nature de la maladie de Basedow," *Bull. et mém. soc. méd. des hôp. de Paris*, 1894, 3 sér. xi. 132-135 , *Mercredi méd.* Paris, 1894, v. 97.—157. *Idem.* *Thèse de Paris*, 1883.—158. MARIE, P., and G. MARINESCO "Coincidence du tabes et de la maladie de Basedow ; autopsie," *Rev. neurol.* Par. 1893 i. 250-255. —159. MARTIN, RAYMOND. *Des troubles psychiques dans la maladie de Basedow*, Par. 1890, 100 pp. No. 376. —160. MARTIUS, F. "Was ist die Basedow'sche Krankheit?" *Berl. Klinik*, 1896, Hft. 95, 1-19.—161. MASOIN, P. "Note sur les modifications de la quantité relative d'oxyhémoglobine contenue dans le sang des myxœdémateux," *Comptes-rend. soc. de biol.* Paris, 1895, 10me sér. ii. 73.—162 MASSARO, D. "Su di un caso di gozzo esoftalmico," *Riforma medica*, Napoli, 1893, ix pt. 4, 507-13.—163. MATHIEU, A. "Un cas de goitre exophth. consécutif à l'ablation des ovaires," *Gaz. des hôp.* lxiii. 70, 1890.—164. MAUDE, A. "Crises of the Digestive Tract in Graves' Disease," *Practitioner*, Lond. 1891, xlvii. 195-197. —165. *Idem* "Œdema in Graves' Disease," *Practitioner*, London, 1891, xlvii. 401-405.—166. *Idem* "Nine Cases of Graves' Disease ; Ophthalmoplegia : Remarks on the Lid-symptoms." *St. Barth. Hosp. Rep.* Lond. 1891, xxvii. 133-148.—167. *Idem.* "A Case of Ophthalmoplegia, with Graves' Disease," *Brain*, Lond. 1892, xv. 121-123.—168. *Idem* "Tremor in Graves' Disease," *Brain*, Lond. 1892, xv. 424-430. — 169. *Idem* "Some Rare Clinical Points in Graves' Disease," *St. Barth. Hosp. Rep.* Lond. 1893,

xxix. 181-88.—170. *Idem.* "On Exophthalmic Goitre," *Brain*, Lond. 1894, xvii. 246-62.—171. *Idem.* "Peripheral Neuritis in Exophthalmic Goitre," *ibid.* 229-31.—172. *Idem.* "Graves' Disease," *Trans. Med. Soc.* 1894, xvii. 12-31.—173. *Idem.* "Tetany in Graves' Disease," *Brit. Med. Journ.* Lond 1896, i 908.—174. *Idem.* "Notes on the Treatment of Graves' Disease by Thymus Gland," *Lancet*, Lond. 1896, ii. 173.—175. *Idem.* "Mental Changes in Graves' Disease," *Journal of Mental Science*, Lond. 1896, xlii. 27-31.—176. Maurice-Faure. "Étude sur le goitre exophtalmique," *Gaz. des hôp.* Par. 1896, lxix. 773-781.—177. Maybaum, J. "Ein Beitrag zur Kenntniss der atypischen Formen der Basedow'schen Krankheit," *Zeitschr. fur klin. Med.* Berl. 1895, xxviii. 112-116.—178. Mendel, E. "Zur pathologischen Anatomie des Morbus Basedowii," *Deutsche med. Wochnschr.* Leipz. 1892, xvii. 89.—179. *Idem.* "Drei Falle von geheiltem Myxodem," *Deutsch. med. Wochenschr.* Leipz. u. Berl. 1895, xxi. 101-103.—180. Middleton, G. S. "A Case of Myxœdema successfully treated with Thyroid Gland; Relapse after Cessation of Treatment and Death from Tumour of the Mediastinum," *Glasgow Med. Journ.* 1894, xlii 430-42.—181. Mobius, P. J. "Ueber die Basedow'sche Krankheit," *Deutsche Zeitschrift f. Nervenheilk.* Leipzig, 1891, i. 400-444.—182. *Idem.* *Die Basedow'sche Krankheit*, Wien, 1896.—183. Montgomerie, H. "A Case of Exophthalmic Goitre, ending fatally, from Sudden Pressure on the Trachea," *Lancet*, 1891, i. 306.—184. Moore, W. O. "Exophthalmic Goitre," *Internat. Clin.* Phila. 1893, 3rd s. i. 92-96.—185. Muller, F. "Zur Kenntniss der morbus Basedowii," *Jahresb. d. schles. Gesellsch. f. vaterl. Kult.* 1890, Bresl. 1891, lxviii. med. Abth. 56.—186. *Idem.* "Beitrage zur Kenntniss der Basedow'schen Krankheit," *Deutsches Arch. f. klin. Med.* Leipzig, 1892-3, li. 335-412.—187. Murray, G. R. "Thyroid Secretion as a Factor in Exophthalmic Goitre," *Lancet, 1893, ii. 1177-1179.*—188. *Musehold, A.* "*Ein Fall von Morbus Basedowii, geheilt durch eine Operation in der Nase,*" *Deutsche med. Wochnschr. Leipz. 1892*, xviii. 93-95.—189. Neustab, J. T. "Morbus Basedowii," *Meditsina*, St. Petersburg, 1892, iv. 289-292.—190. Newman, E. A. R. "The Etiology of Exophthalmic Goitre; a Neurosis; with a Note on Treatment," *Lancet*, 1894, ii. 320.—191. Newton, R. S. "A Case of Exophthalmic Goitre, Thyroidectomy," *Boston Med. and Surg Journ.* 1891, cxxv. 392.—192. Oddo, C. "Un nouveau cas d'idiotie myxœdémateuse traité avec succès par la méthode thyroidienne," *Méd. inf.* Paris, 1895, iii. 3-18.—193. Oliver, T. "The Thyroid and its Diseases; with Special Reference to Exophthalmic Goitre," *Internat. Clin.* Phila. 1893, 3rd s. i. 97-108.—194. Ord, W. M., and E. White. "Observations on a Case of Myxœdema treated by Administration of the Thyroid Gland of the Sheep, with especial Reference to Changes occurring in the Urine," *Trans. Clin. Soc Lond.* 1893-94, xxvii. 37-47, 1 plate.—195. Owen, D. "Thyroid Feeding in Exophthalmic Goitre," *Brit. Med. Journ.* 1893, ii. 1211.—196. Pacheco, R. "Cuatro casos de bocio exoftálmico," *An d. Circ. méd. argent.* Buenos Aires, 1891, xiv. 648-654.—197. *Idem.* "Bócio exoftálmico," *An. d. Circ. méd. argent.* Buenos Aires, 1892, xv. 177-187.—198. Page, R. C. M. "Exophthalmic Goitre," *New York Polyclinic*, 1896, vii. 35-38.—199. Palleske. "Heilung eines operativ enstandenen Myxodems durch Futterung mit Schafsschilddruse," *Deutsche med. Wochenschr.* Leip. u. Berl. 1895, xxi. 103.—200. Passler, H. "Erfahrungen uber die Basedow'sche Krankheit," *Deutsche Zeitschrift fur Nervenheilkunde*, Leipzig, 1894-95, vi. 210-230.—201. Paterson, D. R. "Note on the Etiology of Graves' Disease," *Lancet*, 1894, i. 370.—202. Patrick, H. T. "The Bryson Symptom in Exophthalmic Goitre; with a Report of Forty Cases," *New York Med. Journ.* 1895, lxi. 173-76.—203. Patton, J. M. "Exophthalmic Goitre," *Chicago Clin. Rev.* 1895-6, v. 698.—204. *Idem.* "Graves' Disease," *Chicago Clin. Rev.* 1895-6, v. 424-427.—205. Paul, F. T. *Brit Med. Journ.* vol. ii. 1897, pp. 1-6.—206. Perregaux, E. "Ueber Morbus Basedowii," *Cor-Blatt. fur schweiz. Aerzte*, Basel, 1894, xxiv. 330-343.—207. Peter. "Du goitre exophtalmique," *France méd.* Par. 1892, xxxix. 209-211.—208. Peyron and J. Noir. "Le dermographisme électrique dans le goitre exophtalmique," *Progrès méd.* Paris, 1894, 2 sér. xx. 169.—209. Philipp, A. "Kritische Darstellung der neueren Theorien der Basedow'schen Krankheit," *Allg. med. Centr. Zeitung*, Berl. 1894, lxiii. 457, 469, 481, 493, 505.—210. *Idem.* *Kritische Darstellung der neueren Theorien der Basedow'schen Krankheit*, Berl. 1894, E. Billig, 44 pp.—211. Philippen, J. "L'état de la nutrition de la maladie de Basedow, ses modifications par le traitement thyroidien," *Clinique*, Brux. 1896, x. 409-415.—212. Pisani, Lamberto. *Della tachicardia strumosa esoftalmica*, Stradella, 1891, P. Salvini, 40 pp.—213. Pizzoli, U. "Contributo alla casuistica del morbo di Basedow," *Gazz. d. osp.* Milano, 1892, xiii. 970.—214.

Pospelow, A. "Weitere Beobachtungen über die Behandlung des Myxoedema," *Monatsh. f. prakt. Dermat.* Hamb. 1894, xix. 537-41.—215. **Potain.** "Le goitre exophtalmique," *Revue internat. de méd. et de chir. prat.* Paris, 1895, vi. 365-67.—216. **Poyet, O.** "Goitre vasculaire et suffocant ; traitement par la thyroidothérapie," *Gaz. méd. de Picardie*, Amiens, 1896, xiv. 126-128.—217. **Pribram, A.** "Zur Prognose des Morbus Basedowii," *Wien. klin. Rundschau*, 1895, ix. 689-92.—218. *Idem.* "Zur Prognose des Morbus Basedowii," *Prag. med. Wochnschr.* 1895, xx. 521-523.—219. *Idem.* "Basedow'sche Krankheit," *Prag. med. Wochnschr.* vii. 1882, p. 138.—220. **Putnam, J. J.** "The Treatment of Graves' Disease by Thyroidectomy," *Journal of Nervous and Mental Disease*, N.Y. 1893, xx. 799-821.—221. *Idem* "Notes on Two Additional Cases of Thyroidectomy for Graves' Disease," *Journ. of Nervous and Mental Disease*, N.Y. 1894, xxi. 359-64.—222. *Idem.* "Pathology and Treatment of Graves' Disease," *Brain*, Lond. 1894, xvii. 214-28.—223 *Idem.* "Thyroid Feeding," *Amer. Journ. Med. Sci.* Phila. vol. cvi. pp. 125-148.—224. **Ramsay, A. M.** "Exophthalmic Goitre : a Clinical Study," *Glasgow Med. Journ.* 1891, xxxvi. 81, 178 ; 1 pl.—225. **Raymond** and **Sérieux.** "Goitre exophtalmique et dégénérescence mentale," *Congr. ann. de méd. ment. C.-r.* 1892, Blois, 1893, iii. 198-240.—226. *Idem.* "Goitre exophtalmique et dégénérescence mentale," *Rev. de méd.* Par. 1892, xii. 957-994.—227. **Régis, E.** "Un cas type de myxœdème congénital au début du traitement thyroidienne," *Mercredi méd.* Paris, 1875, vi. 37.—228. **Rehn, L.** "Ueber Morbus Basedowii," *Deutsche med. Wochenschr.* Leipzig u. Berl. 1894, xx. 265-67.—229. **Renaut, J.** [*et al.*] "Corps thyroide et maladie de Basedow ; rapport de M. le Dr. Brissaud," *Courrier méd.* Paris, 1895, xlv. 281-83.—230. **De Renzi, E.** "Sul gozzo exoftalmico," *Riforma Med.* Napoli, 1892, viii. pt. 2, 735, 747, 759.—231. **Riedel, B.** "Chirurgische Behandlung der Basedow'schen Krankheit, Handb. d. spec." *Therap. inner. Krankh.* Jena, 1896, v. 2 Teil, 531-547.—232. **Righi, G.** "Malattia di Basedow e corpo tiroide," *Rassegna med.* Bologna, 1896, iv. No. 5, 3-7 ; No. 6, 4-7 ; No. 8, 1-4.—233. **Ripamonti, A.** "Su alcune forme frusti di morbo di Basedow," *Boll. d. Poliambul. di Milano*, 1892, v. 1-15.—234. *Idem.* "L'estirpazione del gozzo nel morbo di Basedow secondo il Prof. Bottini," *Gazz. med. Lomb.* Milano, 1893, lii. 281-283.—235. **Rockwell, A. D.** "The Treatment of Exophthalmic Goitre, based on Forty-five consecutive Cases," *Med. Rec.* N.Y. 1893, xliv. 417-420.—236. **Rosenblatt.** "Drzenie czlonków (tremor) jako pierwszy objaw choroby Basedowa" [Trembling in the limbs as a phenomenon in Basedow's disease], *Przegl. lek.* Krakow, 1892, xxxi. 440.—237. **Sanarelli.** "Le condizioni attuali delle endemi gozzigene in Italia," *Gior. d. r. soc. ital. d' ig.* Milano, 1895, xvii. 173-92, i. ch. 1 map.—238. **Saundby, R.** "Graves' Disease," *Internat. Clin.* Philad. 1895, 5th ser. ii. 85-91.—239. **Sabrazès** and **Cabannes.** "Guérison rapide d'un goitre simple par l'extrait glycérique de corps thyroide, après l'échec de la médication iodurée," *Gaz. hebd. de méd.* Par. 1896, xliii. 327-329.—240. **Savage, G. H.** "Exophthalmic goitre with Mental Disorder," *Guy's Hospital Reports*, xxvi. p. 31, 1883.—241. **Schenk, Paul.** *Geisteskrankheit bei Morbus Basedowii*, Berl. 1890, G. Schade, 30 pp.—242. **Schmey, F.** "Von der Lebensweisse der an Morbus Basedowii Erkrankten," *Allg. med. Centr.-Ztg.* Berl. 1896, lxv. 257.—243. **Schulte, J. A.** "Exophthalmic goitre ; Anterior Poliomyelitis," *Chicago M. Times*, 1896, xxix 87.—244. **Sharkey, S. J.** "On Graefe's Lid-sign," *Trans. Opth. Soc. United Kingdom*, London, 1890-91, xi. 204-211.—245. **Sibley, K.** "Exophthalmic Goitre," *Clin. Journ.* Lond. 1895, vi. 394.—246. **Sollier, P.** "Maladie de Basedow avec myxœdème," *Rev. de méd.* Par. 1891, xi. 1000-1013.—247. *Idem.* "Un cas de maladie de Basedow ; rapidement amélioré par la galvanisation," *Revue internat. d'électrothérapie*, Paris, 1893-94, iv. 359-62 ; *Revue d'hyg. thérap.* Paris, 1894, vi. 265-68.—248. **Souques, A.** "Note sur l'étendue du champ visuel dans la maladie de Basedow," *Compt. rend. soc. de biol.* Par. 1891, 9 s. iii. 353.—249. **Sottas, J** "Note sur le goitre exophtalmique familial," *France méd.* Par. 1896, xliii. 533.—250. **Spencer, W. F.** "Exophthalmic Goitre with Complications," *Med. Current*, Chicago, 1894, x. 353-55.—251. **Spencer, W. G.** "Exophthalmic Goitre causing Death by Asphyxia," *Brit. Med. Journ.* Lond. 1891, i. 521.—252. *Idem.* "Exophthalmic Goitre in a Girl, causing Death by Asphyxia," *Trans. Path. Soc.* Lond. 1890-1, xlii. 299-301.—253. **Spender, J. K.** "On Points of Affinity between Rheumatoid Arthritis, Locomotor Ataxy, and Exophthalmic Goitre," *Brit. Med. Journ.* Lond. 1891, i. 1169-1171.—254. **Spicer, S.** "Incomplete Graves' Disease with Nasal Polypi," *Lancet*, 1894, ii. 1158.—255. *Idem.*

"A Case of Incomplete Graves' Disease, associated with Nasal Polypi," *Trans. Clin. Soc. Lond.* 1895, xxviii. 265-68. —256. STAFFORD, H. E. "Exophthalmic Goitre," *N. York Polyclin.* 1893, 1, 141.—257. STARR, M. A. "Myxœdema and its Differential Diagnosis from Chronic Nephritis," *Med. News*, Philad. 1894, lxv. 649, 683. —258. *Idem. Med. News*, New York, April 18, 1896.—259. STEINER, D. W. "The Heart in Exophthalmic Goitre," *Trans. Ohio Med. Soc.* Cincin. 1893, 227-31.—260. STEINLECHNER, M. "Ueber das gleichzeitige Vorkommen von Morbus Basedowii und Tetanie bei einem Individuum," *Wiener klin. Wochenschr* 1896, ix. 5-8 —261. STEPPETAT, KARL. *Ueber den galvanischen Leitungswiderstand der Haut bei Morbus Basedowii*, Strassburg, 1890, J. H. E Heitz, 51 pp.—262. STEWART, Sir T. GRAINGER, and G. A. GIBSON. "Bulbar Lesions in Graves' Disease: a Contribution to the Morbid Anatomy of Exophthalmic Goitre," *Edin. Hosp. Reports*, 1894, ii. 275-82, 1 plate. —263. *Idem.* "Clinical Notes on Graves' Disease," *Edinb. Hosp. Rep.* 1893, i. 187-220, 1 pl.—264. STRÜBING. "Ueber mechanische Vagusreizung beim Morbus Basedowii," *Wiener med. Presse*, 1894, xxxv. 1713-17.—265. TAYLOR, J. M. "Abstract of Notes on the Treatment of Exophthalmic Goitre," *Journ. Amer. Med. Assoc.* Chicago, 1893, xxi. 488.—266. *Idem.* "The Treatment of Exophthalmic Goitre," *Med. News*, Philad. 1893, lxiii. 673; 711.—267. THEILHABER, A. "Die Beziehungen der Basedow'schen Krankheit zu den Veranderungen der weiblichen Geschlechtsorgane," *Archiv fur Gynakol.* Berlin, 1895, xlix. 57-74.—268. THOMPSON, J. C. "Notes of a Case of Exophthalmic Goitre," *Pittsburgh M. Review*, 1892, vi. 197 —269. THOMSON, W. H. "The Pathology and Treatment of Graves' Disease." *N. York M. J.* 1893, lvii. 601-605.—270. TOMPKINS, E. L. "Exophthalmic Goitre," *Am. Journ. Obst.* N.Y. 1893, xxviii. 669-680.—271. TOULOUSE, E. "Les rapports du goitre exophtalmique et de l'aliénation mentale; les aliénés à séquestrations multiples; le traitement chirurgical de l'idiotie," *Gaz. des hôp.* Par. 1892, lxv. 1405-1410 —272. "Traitement du goitre exophtalmique," *Union méd.* Par. 1896, 4 s. ii 301-306.—273 TROSCHKE, CARL *Casuistische Beitrage zur Aetiologie und Symptomatologie des Morbus Basedowii*, Greifswald, 1893, J Abel, 26 pp.—274. VANDERVELDE and LE BŒUF. "Le goitre dans la maladie de Basedow," *Journ. de méd. chir. et pharmacol.* Brux. 1894, 129-133. —275. VERCO, J. C. "Myxœdema," *Australas. Med Gazette*, Sydney, 1894, xiii. 156-59.—276. VIGOUROUX, R. "Traitement du goitre exophtalmique par la faradisation," *Gaz. des hôp.* Par. 1891, lxiv. 1291; *Gaz. d. hôp.* Paris, 1891, lxiv. 1325-27.—277. *Idem.* "Le traitement électrique du goitre exophtalmique; sa technique opératoire," *Gaz. d hôp.* Par. 1891, lxiv. 494.—278. *Idem. Gaz. des hôp.* vol. lxiv. p. 140; *Prog. méd.* vol. xv. p. 43, 1887.—279. VOLKEL, ADOLF. *Ueber einseitigen Exophthalmus bei Morbus Basedowii*, Berl. 1890, W. Rower, 35 pp.—280. VOSSIUS, A. "Ein Fall von Forme fruste des Morbus Basedowii," *Beitr. z. Augenheilkunde*, Hamb. u. Leipz. 1895, xviii. 86-92, 2 plates.—281. WALLACE, T. H. "Exophthalmic Goitre," *West. M. Reporter*, Chicago, 1892, xiv. 121-123.—282. WATERMAN, O. M. "A Peculiar Case of Graves' Disease," *Milwaukee Med. Journ.* 1895, iii. 15.—283. WEILL, A., and S. DIAMANTBERGER. "Goitre exophtalmique et rheumatisme," *Bull. soc. de méd. prat. de Par.* 1891, 582-596.—284. WEST, S. "Two Cases of Exophthalmic Goitre in Sisters with Morbus Cordis and a History of Rheumatic History in both," *Lancet*, 1895, i. 1248 —285. WETTE, T. "Beitrag zur Symptomatologie und chirurgischen Behandlung des Kropfes sowie uber die Abhangigkeit des Morbus Basedowii vom Kropfe," *Archiv f. klin. Chir.* Berl. 1892, xliv. 652-716.—286. WIENER, JULIUS. *Ueber einen Fall von Morbus Basedowii mit Tabes incipiens*, Berl. 1891, O. Franche, 31 pp.—287. WILLIAMSON, R. T. "On Prognosis in Exophthalmic Goitre," *Brit. Med. Journ.* vol. ii. 1896, p. 1373 —288. WINCKLER, E. "Zur Beantwortung der Frage; wann Konnen intranasale Eingriffe beim Morbus Basedowii gerechtfertigt sein?" *Wien. med. Wochnschr.* 1892, xlii. 1521, 1556, 1593, 1640, 1676 —289. WINTER, H. L. "The Effects of Thyroid Extract in the Treatment of Graves' Disease," *Am. Med. Surg. Bull.* N.Y. 1896, x. 40.—290. WOOD, H. C. "Graves' disease. Case I.: Spontaneous cure occurring during abscess of spleen. Case II.: Very great relief apparently from the use of extract of spleen," *Univ. Med. Mag.* Philad. 1894-95, vii. 318.

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DISEASES OF THE SPLEEN

THE GENERAL PATHOLOGY OF THE SPLEEN.—*General Remarks. Effects of splenectomy in man. The condition of the spleen in bacterial infection and in toxæmia. The part of the spleen in bacterial infection and in immunity. The part of the spleen in the various forms of anæmia.*

General remarks.—From a consideration of their structure and functions the ductless glands may be divided into two categories—(i.) those of an epithelial type which have an internal secretion, such as the thyroid, suprarenal, and pituitary glands; and (ii.) those containing lymphoid tissue which are not known to possess any special internal secretion—the spleen and the thymus gland.

There appears also to be a general difference in their pathological relations; the spleen and thymus are affected and undergo alteration rather as the result of disease elsewhere than as its cause; while in the case of the thyroid, suprarenal bodies, etc., we have chiefly to deal with primary morbid conditions and diseases, such as myxœdema or Addison's disease, initiated in these organs, which lead to general and secondary changes elsewhere. It would be unwise, in the present state of our knowledge, to press this distinction too far, and to assert too dogmatically that there is not such a thing as primary disease of the spleen; for until our knowledge of the physiology of the spleen is in a more satisfactory state the problems of its pathology must necessarily present great difficulties. But we may safely consider the spleen as an organ prone to respond to disease of other parts, especially of the blood and the hæmatopoietic organs of the body, and but little liable to independent primary affections.

The two diseases in which the spleen has most claim to be regarded in the initiation of morbid processes are splenic or spleno-medullary leukæmia and splenic anæmia. With regard to splenic leukæmia, the most careful observations point strongly to the conclusion that the primary seat of the disease is in the marrow of bone, and that the splenic changes are merely secondary.

With regard to splenic anæmia, we are not at present in a position to decide dogmatically whether the marked morbid appearances in the spleen are primary or whether they are secondary and perhaps the result of a chronic toxæmia; but the second alternative seems the more reasonable. (*Vide* art. "Splenic Anæmia" in the following volume.)

Effects of splenectomy in man.—A point of some interest is whether atrophy of the spleen, as distinguished from removal, may give rise to compensatory changes in lymphatic glands and the red marrow of bone, and to leucocytosis such as may be produced by splenectomy. Whether primary changes in the spleen, as a compensatory effort, and subsequent functional inadequacy of the organ ever give rise to hypertrophy of other forms of hæmatopoietic tissue, we do not know; at any rate, this sequence has not been established.

That the spleen is not essential to life, and that its removal does not affect development, has been shown experimentally in animals and as the result of splenectomy in human beings; whether for disease of the organ or for traumatic rupture. During the course of disease compensation gradually takes place, and when the organ is subsequently removed the results are less marked than they are when a previously healthy organ is removed and compensation has to be effected suddenly.

In splenic anæmia the changes in the spleen are associated with well-marked symptoms, so that compensation cannot be said to have taken place, and it is noteworthy that the lymphatic glands are not enlarged; whereas after removal of a healthy spleen there is anæmia for a time, as in splenic anæmia; but compensation is effected by enlargement of lymphatic glands and leucocytosis, probably also by extension of the blood-forming marrow into the shafts of the long bones; and eventually recovery occurs.

Pitts and Ballance successfully removed the spleen for traumatic rupture in three cases: the first was a boy in whom a splenunculus was left behind, and in whom no special symptom except glandular enlargement followed the operation; a somewhat similar case of Reigner's is quoted, and it is suggested that the more extensive presence of red marrow in youth may explain this. Compensatory hypertrophy of the splenunculus may also have played some part in bringing this about. The other two cases, a woman aged 45 years and a man aged 36, presented the following definite group of symptoms—

(i.) Progressive loss of strength and of weight and emaciation.
(ii.) Extreme anæmia.
(iii.) A daily rise of temperature from 1° to 3° Fahr.
(iv.) Increased frequency of the pulse.
(v.) Fainting attacks, with increased pallor of the surface.
(vi.) Headache, drowsiness, great thirst.
(vii.) Severe griping pains in abdomen, and pains in the legs and arms; in the woman tenderness along the tibiæ, thought to indicate compensatory changes in the red marrow of bone.
(viii.) Enlargement of the external lymphatic glands, which remained permanently.
(ix.) Blood changes, diminution in the number of the red blood corpuscles, increase in the number of leucocytes. In both cases a month after operation the hæmoglobin was found to be half the normal.

Convalescence was very slow, but recovery with return to normal weight eventually occurred.

Many of these changes correspond with the experimental results obtained by Laudenbach in splenectomy in dogs.

Splenectomy in man for the enlargement of malaria, for wandering spleen, and for other morbid conditions except leukæmia, may give rise to temporary changes in the blood, and very occasionally to temporary enlargement of the lymphatic glands; but not to the more marked results seen when a previously healthy organ is removed for rupture. This perhaps is due to the gradual establishment of compensation during the progress of the disease. For in wandering spleens endarteritis and thrombosis of the splenic vessels are apt to occur as the result of torsion of the elongated pedicle; this leads to atrophy of the Malpighian bodies, and to sclerotic and fatty changes in the pulp. An organ so altered would be of but little use in the economy, and compensation would have taken place before the performance of splenectomy.

In a case of wandering spleen in which Mr. Ballance performed splenectomy symptoms of much severity occurred; but this exceptional sequel was probably explained by the fact that the spleen appeared quite healthy, and so, presumably, no compensation being required none had taken place.

The spleen in bacterial infection and in toxæmia.—In acute fevers and in bacterial infection there is a general tendency to an accumulation of micro-organisms in the spleen; this, for example, is especially well marked in septicæmia, infective endocarditis, and enteric fever. The micro-organisms found in the organ are by no means limited to the one giving rise to the specific disease; thus in typhoid fever streptococci and staphylococci may be present. Some of the microbes are free, others are enclosed in cells.

It does not follow, however, that because micro-organisms are found in the spleen that they are necessarily present in the blood. In enteric fever, for example, while they are constantly present in the spleen, they are only to be found in the general circulation under exceptional conditions.

This microbic occupation is accompanied by well-marked hyperæmia and swelling of the organ, even to such an extent that in rare cases rupture has occurred spontaneously. In children the capsule of the spleen is more extensible than in older people, and the enlargement therefore is relatively better marked. This condition is sometimes spoken of as acute splenic tumour. On section the spleen is soft and the pulp is sometimes so diffluent as to run away. In some experiments on pneumococcal infection in rabbits Washbourn found that the spleen might be either softened, as here described, or firm and normal in consistency. This latter condition may somewhat exceptionally be met with in man; in cholera the spleen is firm and somewhat diminished in size, probably from the concentration of the blood.

In bacterial infection the colour of the spleen on section is either that of marked congestion, or grayish from increase of leucocytes in its substance. The Malpighian bodies are prominent and swollen in some cases, while in others they can only be seen with difficulty. In addition to the accumulation of micro-organisms in the spleen, changes in its histological structure occur; these are due to the effects of the toxic products of bacterial activity. That they are independent of the presence of bacteria in the organ is shown by the fact that they follow the injection into the circulation of toxalbumins only.

The Malpighian bodies when affected are swollen and enlarged, and by proliferation of their constituent cells leucocytosis and phagocytosis are forwarded. The cells become swollen, granular, and may show the nuclear changes of fragmentation due to degeneration set up by the toxalbumins. As a result of the concentration of toxins, focal necroses of the cells, either in the centre of the Malpighian bodies or in the pulp, may follow; this is well marked in relapsing fever, and may be seen in enterica.

The pulp becomes engorged with blood and may contain hæmorrhages; while numerous cells, macro- and microphages containing blood corpuscles and bacteria, are visible. A similar phagocytic action may be taken on by the endothelial cells lining the sinuses, which in places may show similar degenerative changes to those seen in the areas of focal necroses. Fibrinous thrombi may form in the capillaries of the splenic pulp.

The degenerative changes may eventually lead to some degree of atrophy of the splenic tissue, to hyaline degeneration of the small arteries, and to fibrosis.

In scarlet fever Klein described multiplication of the muscular fibres and hyaline degeneration of the arterial walls, leading to their occlusion; while the adenoid tissue around undergoes the same hyaline degeneration. In typhoid fever also inflammatory changes in the arteries have been noted. The proliferative, vascular, degenerative and necrotic changes that take place in the spleen in bacterial infection may be broadly described as inflammatory, and the condition as a form of splenitis; but it is noteworthy that in the infectious fevers the condition rarely goes on to suppuration such as is frequently seen in pyæmia, where a further determining factor is provided by embolism and infarction.

If, as seems *a priori* reasonable, the hyperæmia and consecutive changes in the spleen in bacterial infection are due to the products of bacterial activity, it would be natural to expect that in cases of sapræmia and in toxæmia a somewhat similar change would occur in the spleen.

The specific albumoses of diseases have been obtained from the spleen by Dr. Sidney Martin and others in cases where no micro-organisms were present in the organ. Here the poisons are carried to the spleen by the blood, while in general hæmic infection they are manufactured on the spot.

That the organ is invariably enlarged in toxæmia, apart from the presence of bacteria in the spleen, is contrary to experience; but in pneumonia, where the diplococci are very rarely present in the blood or in the spleen, the spleen is softened or enlarged, and the same is true of some cases of sapræmia; while in some conditions, probably or possibly of this nature—such as Hanot's hypertrophic cirrhosis with chronic jaundice, the early stages of syphilis, Landry's paralysis, and exophthalmic goitre—the organ is enlarged.

Flexner, in an experimental study of the tissue changes produced by the injection into the circulation of ricin and abrin, phytalbumoses obtained from the seeds of the castor-oil plant and the jequerity bean (Abrus precatorius), found the spleen uniformly swollen and soft, the swelling apparently being of the splenic pulp. While bacterial toxalbumins affect the Malpighian bodies more than the pulp, the reverse is the case with ricin and abrin intoxications. In chronic poisoning with these phytalbumoses the splenic pulp is crowded with granules and globules of yellow pigment occurring inside the cells. This pigment gives a blue colour with ferrocyanide of potassium and hydrochloric acid, and is to be regarded as the evidence of great hæmolysis. As a result of poisoning dogs with metatoluylendiamin, paraphenylene and nitrate of soda, Pilliet (43) found that the Malpighian bodies become atrophied, and thus that a kind of cirrhotic atrophy results.

On the other hand, in uræmia, the most familiar example of a purely chemical toxæmia, no splenic enlargement occurs.

In considering these discordant data, it must be borne in mind (*a*) that the effects of various poisons are likely to be different, and (*b*) that in toxæmia the poison reaches the spleen in a very dilute form when compared with its relative concentration when the spleen is occupied by active micro-organisms.

We can only conclude that in toxæmia the spleen may be affected in the same way as in bacterial infection, though by no means constantly.

As a result of long-continued bacterial infection, or toxæmia, the spleen may show a varying degree of fibrosis.

The part of the spleen in bacterial infection.—The spleen is, generally speaking, so altered in fevers and in cases of bacterial infection, that the question naturally arises whether this is merely a secondary change, or whether special and defensive processes take place in the spleen, whose object is to protect the organism against the infection.

Does the spleen play any special part in the defence of the organism which is distinct from that played by lymphatic tissue elsewhere?

In cases of general hæmic infection the spleen and liver are perhaps the organs most extensively occupied by the micro-organisms. This is well seen in anthrax and in streptococcal septicæmia. Is this merely a stagnation of the microbes in the lax, open tissue of the spleen? Or is there in addition a multiplication of the microbes and a manufacture of toxins and bacterial products in the spleen, so that renewal of the organ might diminish the toxic process? The observation that in malaria splenectomy is followed by a diminished toxicity of the urine (Jonnesco) lends some support to this hypothesis.

Or, on the other hand, is an extensive destruction of micro-organisms taking place in the organ?

Or are both these processes going on? If so, the spleen is, so to speak, the battlefield where the struggle between the invading micro-organisms and the defensive powers of the body is fought out?

That the spleen is a kind of resting-place into which micro-organisms, which have gained an entrance into the blood, may get swept and left is shown by injecting harmless microbes into the circulation of an animal. They rapidly disappear from the circulation, but may be found weeks after stowed away in the spleen, liver, and marrow of bone.

As has been already seen, the Malpighian bodies of the spleen contain lymphoid tissue, and show proliferative changes in bacterial infection leading to leucocytosis.

Metschnikoff, indeed, regarded the spleen as a centre for the manufacture of phagocytes, and of their presence there can be no doubt. Hankin and others have obtained a bacterial substance from the spleen which is the same as the tissue fibrinogen of Wooldridge, or Halliburton's nucleo-albumin obtained from lymphatic glands, liver, kidney, and so on.

The question to be answered is, whether the spleen has any protection or defensive power other than that possessed by the lymphoid or other tissues generally.

In order to determine whether the spleen plays a special part in *natural immunity*—in the defence of the organism against infection—numerous experiments on animals have been performed.

Bardach came to the conclusion that removal of the spleen renders the animal less resistant to infection; an effect attributed to a diminution of the area of phagocytosis. This writer considered that the part of the spleen in infections is phagocytic, that micro-organisms are taken up there by macrophages and microphages just as they may be seen to be on the spleen of malaria and relapsing fever, and that they are thus destroyed. Bardach was opposed to the view that in bacterial infection any chemical bactericidal body is manufactured by the spleen.

The part of phagocytosis in immunity has already been discussed in Dr. Kanthack's article in the first volume of this work, and has been shown to be subordinate since it is only one, and even then not a constant factor in the production of immunity [vol. i. p. 567].

On the other hand, to take a few of many examples, Tictine injected the blood of relapsing fever containing the spirillum Obermeieri into the circulation of monkeys whose spleens had been removed, and found, contrary to the results of Soudakewitch and Metschnikoff, that they recovered—though, it is true, not so readily as ordinary monkeys—and that subsequently they became immune.

In like manner Orlandi finds that in rabies splenectomy does not affect the course of the disease in any way, and assumes that it plays no part in the defence of the organism against rabies.

Montouri found that the bactericidal power of the blood of dogs and rabbits remained normal for fifteen days after splenectomy, as shown by its action on typhoid bacilli and the cholera vibrio; that it then diminished and disappeared. This, however, was but a passing phase, and in four months from the splenectomy it had regained its normal power. These changes were more rapid in young than in old animals.

Experiments on rabbits that had been splenectomised, and were, after varying intervals, inoculated with different micro-organisms, led to discordant results. Thus, twenty-five days after splenectomy, a rabbit was less resistant than normal to bacillus pyocyaneus, while it had regained its usual resistance to staphylococcus pyogenes (12).

In a series of dogs and rabbits in which splenectomy was followed by experimental infection with Fraenkel's pneumococcus and the bacillus typhosus, the results were practically the same as in animals similarly infected but whose spleens had not been removed; any slight differences that did occur appeared to depend on variations in the interval between splenectomy and the subsequent infection (23).

In conclusion, it would appear that the spleen has no special functions with regard to natural immunity, and that if it plays any part this can be vicariously assumed by other organs.

Tizzoni and Cattani (59) considered that their earlier experiments show that the spleen plays an important part in *acquired immunity.* They were unable to render rabbits, whose spleens they had previously removed, immune against tetanus. It thus appeared possible that the spleen might have the power of manufacturing some substance necessary to render the organism immune.

Kanthack (30), however, working with rabbits and the bacillus pyocyaneus, found that splenectomy, whether before or after protective inoculation, has no effect on the resulting immunity, and does not interfere in any way with the process, the temperature curve and leucocytosis being unaffected.

Tizzoni and Cattani (60) more recently modified their previous opinion considerably, and came to the conclusion, which Righi also shares, that removal of the spleen merely acts like any other severe lesion, and reduces the general resisting powers of the organism temporarily; but that it does not produce any permanent or specific change in the protective powers of the animal.

From a consideration of all these data, it appears highly probable that the spleen has no special protective power, either in natural or acquired immunity, which cannot be vicariously assumed by other organs, such as the lymphatic glands.

The spleen, in fact, is and behaves like a lymphatic gland broken up and embedded in erectile tissue. The Malpighian bodies and adenoid tissue play much the same part that lymphatic glands do elsewhere; while the open, loose, vascular tissue of the organ serves rather as a filter in which various bodies are deposited by the blood, perhaps to remain, perhaps to undergo subsequent changes.

The part of the spleen in the various forms of anæmia.—Since the spleen is so closely associated with the blood, shares in its changes, and is at least intimately connected with hæmolysis or the destruction of the red blood corpuscles, it is only natural to inquire whether any causal relationship may exist between changes in the spleen and anæmia. If the normal function of the organ be connected with destruction of red blood corpuscles, might not an exaggeration of this function give rise to anæmia?[1]

In traumatic anæmia the spleen, of course, cannot be supposed to play any causal part, while, with regard to the possibility of its playing any compensating part, it is doubtful whether, even in the emergencies of severe traumatic anæmia, the spleen can form red blood corpuscles in adult life, as Bizzozero and others believe.

The part of the spleen in splenic anæmia.—Bruhl regards the change in the spleen as primary, and causing the anæmia; he believes that the atrophy and loss of functional activity of the organ lead to an alteration in the chemical constitution of the blood.

But if the symptoms of splenic anæmia are entirely due to splenic inadequacy, it is manifest that splenectomy in normal individuals should give rise to splenic anæmia. This, however, is not the case. The effects of splenectomy are unimportant compared with those of the disease. After splenectomy in healthy persons and in animals anæmia results; but after a time compensation is established by enlargement of lymphatic glands and by an extension of the epiphyseal bone marrow into the shafts of the long bones, and the anæmia passes away; whereas in splenic anæmia compensation does not occur, and the disease does not tend to gradual spontaneous cure.

These considerations render it highly improbable that splenic anæmia is simply due to splenic inadequacy.

It has been thought, however, that splenic anæmia may be due to some morbid process originating in the spleen; and in support of this view it might be urged that in a few cases of the disease removal of the spleen led to a decided improvement. The improvement that has been noticed in splenic anæmia after splenectomy can be explained quite apart from the view that the change in the spleen is the essential cause of the anæmia. Hunter (27) found that in rabbits, after removal of the spleen, toluylendiamin no longer gives rise to hæmolysis, or only to a very slight degree. Bottazzi, from experimental data, concludes that normally the spleen loosens the cohesion between the hæmoglobin and the red blood corpuscles; this he calls the hæmokatatonistic function of the spleen. When the spleen is removed the red blood corpuscles thus become more stable than normal.

In accordance with this view, if splenic anæmia is a chronic intoxication, removal of the spleen would thus diminish the hæmolysis due to the action of a poison, by rendering the red corpuscles less vulnerable. This view would also explain the sequence of events in a case reported by Dr. Coupland: a woman suffering, apparently, from splenic anæmia was much benefited by splenectomy, but after death most pronounced syphilitic disease of the liver was found. Here splenectomy may simply have prevented the toxic anæmia due to the syphilitic virus.

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[1] For a full account of splenic anæmia see article in vol. v.

There is no satisfactory evidence to show that splenic anæmia is due to loss of functional activity of the spleen, or to any primary morbid change originating in the organ.

Is there any evidence to show that splenic anæmia is the result of an exaggerated activity of the hæmolytic function of the spleen? This seems improbable, since the increased size of the organ is not due to hypertrophy, but to cirrhotic atrophy of the splenic tissue. Moreover, the spleen usually does not contain much pigment or show the reaction for free iron, which might be expected if excessive hæmolysis were taking place in the organ.

If neither loss of functional activity nor exaggerated hæmolytic activity of the spleen be the cause of splenic anæmia, it would appear that the change in the spleen is not primary, and that it and the other symptoms—hæmolysis, anæmia, debility, and so forth—may be the results of some common cause or causes of chronic toxæmia, for example; the effects of this cause being first seen and most marked in the spleen, and subsequently in the blood, as shown by anæmia; and often in the liver, as shown by cirrhosis.

The appearances in the spleen are quite compatible with chronic infection or intoxication, and, indeed, rather suggest it; but of its existence there is no definite proof, since no micro-organisms or blood parasites have been found to explain the condition.

In chlorosis all the evidence is to show that the formation of red blood corpuscles, and especially of hæmoglobin, is at fault, and there are no grounds for thinking that increased blood-destruction plays any part. The theory of fæcal anæmia, originated by Sir Andrew Clark, has been shown by Dr. Stockman to rest on no basis of fact; the processes of decomposition in the intestinal tract and of hæmolysis being less than in normal conditions.

Laudenbach's recent experiments and observations on the effects of splenectomy in dogs lead him to conclude that the spleen takes a part in the manufacture of hæmoglobin and in the complete formation of red blood corpuscles. But this does not throw any light on the causation of chlorosis, since the only changes seen in the spleen in that disease are clearly the results of the general anæmia.

In pernicious anæmia it is perhaps less unlikely that the spleen may play an active part in the production of the disease, but there is as yet no absolute proof that it does so. The discussion of the subject is rendered extremely difficult by the fact that our ideas of pernicious anæmia are but a mass of shifting hypotheses. Much will depend, therefore, on the view taken of the nature and cause of pernicious anæmia. If it be regarded as merely an exaggerated form of a hæmogenetic anæmia like chlorosis, and due to a failure in blood-production; or if with Stockman it be regarded, not as a special disease, but as a congeries of symptoms caused by many diseases and intensified by the effects of multiple internal hæmorrhages, the spleen cannot be thought to be in any way responsible. But if Hunter's view be adopted, that pernicious anæmia is essentially hæmolytic in nature, and due to destruction of the red blood corpuscles in the portal system by means of a poison absorbed from the alimentary canal, we may ask whether the spleen plays any part in the process. In normal conditions the spleen, though this is far from being universally accepted, is one if not the chief seat of blood-destruction. When there is an exaggerated hæmolysis going on in the portal system, does the spleen play any special part?

Examination of the spleen itself in pernicious anæmia does not lend support to the hypothesis that the abnormal blood-destruction takes place solely in that organ. Hunter (26), while mentioning four cases in which its weight varied between 10 oz. and 19 oz., says that in the majority of cases its weight is either normal or not mentioned; and in some cases its weight is certainly very much reduced indeed. It has indeed been thought that any enlargement is accidental and due to factors connected with the disease, such as fever, rather than to increased functional activity. The appearances of the pulp are various. Hunter (27) insists on the large amount of pigment, which is only excelled by that seen in malaria. But, even though the amount of pigment (hæmatosiderin) be increased, this fact could not prove that excessive hæmolysis had taken place in the spleen; for the products of blood-destruction arising elsewhere, like foreign bodies such as coal dust or particles of carmine, are commonly carried to the spleen and deposited therein. This process may lead to what is called a spodogenous enlargement of the organ. Microscopically there is, as a rule, no marked change in the spleen; occasionally nucleated red blood corpuscles have been seen, but they are compensatory and due to the anæmia, not in any way accountable for it. It cannot be said that there is any positive evidence to prove that in pernicious anæmia there is excessive hæmolysis limited to the spleen. But although pernicious anæmia cannot be shown to be due solely to exaggerated hæmolysis on the part of the spleen, it is still quite conceivable that the spleen plays some part in this abnormal hæmolysis, just as it does, in all probability, under normal conditions.

Hunter (27) has shown that after removal of the spleen the injection of toluylendiamin into the blood of rabbits is no longer followed by great blood-destruction; hæmolysis, indeed, is either abolished or greatly reduced, so that the presence of the spleen appears to be necessary for the hæmolytic action of this poison, which under normal conditions is well marked. Experimenting on dogs, Bottazzi found that three days after splenectomy the red blood corpuscles parted with their hæmoglobin much less readily than before the operation. This effect lasts a long time. He concludes that, side by side with its function of destroying red blood corpuscles, the spleen has the power of rendering hæmoglobin more readily separable from the red blood corpuscles. This function of the spleen he calls hæmokatatonistic.

That the spleen has some such action appeared probable from

Hunter's experiments just quoted; and Gabbi found that after splenectomy in guinea-pigs the count of red blood corpuscles was increased, though in rabbits splenectomy had no effect.

If we admit that the actual hæmolysis in pernicious anæmia is the effect of a toxin absorbed from the alimentary canal, the hæmokatatonistic action of the spleen would render this destruction more easy, while atrophy of the organ or its removal should have the opposite effect.

Bottazzi, in animals rendered anæmic experimentally, found the red blood corpuscles more tenacious of their hæmoglobin than normally; that is, in much the same condition as after splenectomy. This he explained by supposing that in extreme anæmia the spleen attempts to compensate the blood change by forming red blood corpuscles (Bizzozero), and that while so doing it loses its hæmokatatonistic power. This observation and hypothesis have no bearing on pernicious anæmia; for it is well known, as Copeman showed, that in pernicious anæmia the hæmoglobin leaves the red blood much more readily than normal. This last fact is rather in favour of an exaggeration of the hæmokatatonistic action of the spleen in the disease, but whether this be so we have no further evidence at present.

In conclusion, there is no evidence that the spleen plays any part at all in the production of chlorosis or of traumatic anæmias; but it appears possible that in pernicious anæmia it plays an accessory though not the chief part in hæmolysis. Caution is, however, most necessary in forming any positive opinions on the pathology of pernicious anæmia in the present state of our knowledge.

SPECIAL PATHOLOGY

Malformations:—Atrophy; post-mortem changes.
Capsulitis.
Chronic venous congestion.
Hæmorrhages.
Cysts.
Infarcts.
Abscess.
Tubercle.
Syphilis.
Rickets.
Lardaceous disease.
Malignant disease.

Malformations.—Under this heading reference may conveniently be made to anatomical abnormalities in conformation, including the presence of accessory spleens, and to changes in the position of the organ.

Very considerable physiological variation may exist in the outline of the organ; sometimes it is found to be elongated, and to resemble the form met with in some animals: at other times it is more compressed and rounded than usual.

The outline of the anterior margin may show a number of notches which, in enlargement of the organ, may become very accentuated; occasionally a deep notch may even partially divide the spleen into two. Under ordinary conditions there may be a single slightly-marked notch on the anterior border near its lower end; but it is variable in its position, and even may occur on the posterior margin, or be absent altogether. Dr. A. Latham has shown me a most remarkable abnormality of the spleen found in the post-mortem room of St. George's Hospital. The spleen gave off a long process which was bound down to the posterior abdominal wall by the peritoneum and ran down into the left side of the scrotum. In thickness it was equal to the little finger. Microscopically it was composed of splenic tissue. It was probably carried down in the descent of the testes, just as accessory suprarenal bodies may be transported into the neighbourhood of the epididymis.

Accessory spleens, splenunculi or lienculi, are common; they occur in the folds of peritoneum passing to the spleen, the gastro-splenic omentum, and left pancreatic gastric fold, in the great omentum on the left side, and even between the layers of the costo-colic fold of peritoneum or suspensory ligament of the spleen. Usually they are close to the hilum of the spleen, and are not more than one, two, or three in number; but as many as thirty or forty have been found.

It is generally thought that accessory spleens are commoner in early life. Jolly, in eighty post-mortem examinations of patients under sixteen years of age, found them in twenty, or one in four; but they became more frequent as age advanced. It may be that though more manifest in children they are not really more frequent. It has been stated that accessory spleens are commoner in the south of Europe than in the north.

Mr. Bland Sutton says that, especially in cases of transposition of the viscera, the spleen may be represented by a number of splenunculi, which may be clustered together like a bunch of grapes or be more widely separated.

Albrecht has described a case in which an enormous number of accessory spleens, varying in size from a hazel-nut to a pin's head, were found scattered all over the peritoneum; in the situation of the spleen there was one as large as a walnut; microscopically they were composed of splenetic tissue much pigmented.

The existence of these accessory spleens admits of two explanations: some of them, those in the hilum of the organ, are probably separated from the main body of the organ, a projecting tongue becoming pedunculated, and, finally, connected by blood-vessels only; others, those in the great omentum, may with probability be regarded, like suprarenal "rests," as isolated and outlying fragments of the mesoblastic tissues destined to form the main organ. Like other "rests," they may become indented and embedded in other organs; thus Dr. Biggs has described an accessory spleen in the tail end of the pancreas.

If accessory spleens become indented on the surface, and subsequently embedded in the substance of the spleen, they may form encapsuled tumours in the organ. From the fact that in fœtal life the left lobe of the liver and the spleen are in contact, it might naturally be expected that an accessory spleen might become indented and implanted in the surface of the liver, but this does not appear to have been observed.

They undergo the same changes as the main organ. In a case of splenectomy in a boy for rupture, recorded by Ballance and Pitts, an accessory spleen was left, and by compensatory hypertrophy may have had some share in preventing the symptoms following removal of the organ which were noticed in the other two cases of splenectomy for rupture recorded by these observers. Experimentally, after removal of the spleen numerous small red masses have occasionally been found in the omentum; they contained nucleated red blood-cells, but there is some doubt whether they are, as was first stated, composed of characteristic splenic tissue. Laudenbach found them in a splenectomised dog, in which the usual compensatory extension of red marrow into the shafts of the long bones had not occurred, and he considered that they were mesenteric glands which had taken on the formation of red blood corpuscles in lieu of the red marrow.

Congenital absence of the spleen is very rare in bodies otherwise normal; it has been noted in monsters. Garrod, in a paper on the association of cardiac malformations with other congenital defects, refers to two cases of congenital morbus cordis in which the spleen was entirely absent; in two other cases it was multiple, there being nine and four spleens respectively.

In complete situs transversus the spleen is present on the right side of the abdomen. In cases of congenital or traumatic diaphragmatic hernia the spleen readily passes into the left pleural cavity.

Atrophy.—In old people the spleen, like the other lymphoid tissues, undergoes atrophy, sometimes to an extreme degree; so that instead of its normal weight of 7 oz. it weighs only a few drachms. The same condition of atrophy occurs in cases of very chronic diseases.

The capsule is shrivelled, thrown into folds, and somewhat opaque, the substance of the organ is soft and pale; and from atrophy of the pulp the vessels and trabeculæ stand up prominently. In cases of simple atrophy there is no increase of pigment, but, if there has been any disease giving rise to extensive hæmolysis, the substance of the organ may be deeply pigmented. Microscopically there is atrophy of the Malpighian bodies and of the pulp of the spleen, while the arteries show arteriosclerosis, and the pulp is seen to be undergoing atrophy. A rather firm fibrotic form of atrophied spleen is said to be associated with arteriosclerosis in the aged. This form of atrophy occurring in senile and marasmic conditions may be spoken of as simple.

There are cases, however, in which, although increased in bulk and weight, the spleen shows a replacement of its essential elements—the pulp and Malpighian bodies—by fibrous tissue. Such a change occurs in splenic anæmia and in chronic lymphadenoma—conditions probably due to some form of chronic toxæmia. The spleen cannot, in ordinary parlance, be said to be atrophied, but functionally it is much in the position of an atrophied organ. In this connection Pilliet's (43) experiments are of considerable interest. He found that on dogs poisoned by metatoluylendiamin, paraphenylene, and nitrate of soda the Malpighian bodies became atrophied, and the splenic pulp distended with blood; these changes he regards as characteristic of the senile spleen.

Post-mortem changes.—Two very evident alterations which occur after death may be referred to.

(i.) When the stomach or colon contains much flatus, the surface of the spleen in contact with them is often found to be of a black or purple-green colour. The change is not present throughout the organ as it is in melanæmia, but it is limited to the areas of contact with the hollow viscera, and on section is seen to be quite superficial. A similar appearance may often be found on the surface of the liver. It is due to gases, among which is sulphuretted hydrogen, diffusing through the walls of the stomach and intestines after death, and meeting in the spleen with traces of iron contained in hæmatosiderin, and derived from hæmoglobin; as a result of this reaction sulphide of iron is produced.

(ii.) Occasionally the spleen is found honeycombed by small gas-containing cysts. This emphysematous condition, when present, is usually found in cases fatal from microbic infection, such as pyæmia. It is, however, less marked in the spleen than in the liver; to the latter condition the term foaming liver (1) has been applied. Welch and Flexner have shown that this condition is due to the activity of the bacillus aerogenes capsulatus. The infection is secondary, and is a post-mortem or agony phenomenon. Adami doubts whether, under ordinary conditions, this bacillus can grow in the human organism without the simultaneous presence of aerobic microbes. Kanthack has found that the bacillus coli communis may also give rise to this emphysematous condition.

Capsulitis is a convenient and comprehensive term for a group of pathological changes which are of but little clinical importance, though pain in the left side and stitch may be explained by their presence. Under this heading we may include (i.) adhesions, the result of some past attack of peritonitis, local or general; (ii.) chronic peritonitis involving the whole or greater part of the peritoneal covering of the organ; and (iii.) the local thickenings, or lamellar fibromata, so commonly met with on the surface of the organ.

(i.) *Adhesions* round the spleen uniting it to the diaphragm, abdominal wall, stomach, or colon, may follow a past attack of acute peritonitis. These adhesions are vascular, and, of course, vary in their extent and firmness. Sometimes they may be filamentous and easily broken down; they may, in fact, become torn across as the result of abdominal movements, and then appear as small loose tags on the surface of the organ. Occasionally they are so small at their point of attachment to the surface of the spleen as at first sight to resemble miliary tubercles. In other cases the adhesions may be so firm as to suggest recurrent attacks of inflammation or a prolonged inflammatory condition.

Very frequently local adhesions around the spleen are present without any other signs of past inflammation of the peritoneum. In such cases it will frequently be found that there are firm adhesions at the base of the left lung; presumably a past pleurisy or pneumonia had given rise to an inflammation of the diaphragm and of the peritoneum around the spleen.

In other cases local adhesions may be due to some cause originating within the spleen itself. The infarcts so frequently met with in the enlarged spleen of leukæmia often set up local peritonitis. The same thing occurs with infarcts secondary to endocarditis. Similarly, tubercle or lymphadenoma, or the enlargement and attacks of congestion of an ague cake spleen, may be the cause of local peritonitic adhesions. Mr. Henry Morris has told me of several cases operated upon by himself in which on freeing peritoneal adhesions around the spleen a remarkable and rapid diminution in its size had taken place. In such cases the adhesions first became organised when the spleen was enlarged, and as the result of the permanent traction exerted by them the organ was held open and unable to contract.

(ii.) *Chronic peritonitis* attacking the whole or the greater surface of the organ is generally but a part of general chronic peritonitis (compare article on "Perihepatitis"). Chronic capsulitis or perisplenitis may, however, be independent of this general cause, and be due to some local lesion of the spleen, such as a gumma.

The macroscopic appearances are very characteristic. The organ is tightly shrouded in a firm, opaque membrane of almost cartilaginous consistency. Often, but by no means always, this fibrous membrane can be peeled off, so as to expose the peritoneal surface of the spleen. The outer surface of this "false" membrane is fairly smooth, but not uniform, for scattered irregularly over it there are round depressions resembling the impress of rain-spots on soft sand. Their presence can be best explained by supposing that, after the formation of this inflammatory tissue, cicatricial contraction took place, and that, as a result of the increased tension thus brought about, the membrane had ruptured, either at its weakest spots or where the tension was greatest. This condition of chronic capsulitis may be accompanied by adhesions to the adjacent parts, but they are often absent.

(iii.) *Localised thickenings on the peritoneal surface of the spleen* are one of the commonest post-mortem appearances. They closely resemble the thickenings sometimes seen over the apices of the lungs, and may be compared with the "milk-spots" so commonly present on the pericardium. They may be aptly described as corns due to attrition. They are not met with on the surface of the liver, or indeed elsewhere on the peritoneum, except as a result of some definite local irritation. An admirable example of a similar formation occurring in the subperitoneal tissue covering the rectum, and due to the irritation of a piece of iron, has been described by Mr. Shattock (44).

The anterior surface of the liver often presents an opaque and thickened condition of the peritoneum due to tight lacing or to the friction of a hypertrophied heart; but these thickenings, which resemble the milk-spots on the heart, are not the exact counterpart of the lamellar fibromata on the spleen with which we have compared them. They are not so localised, and not nearly so massive.

Their frequent occurrence on the capsule of the spleen is probably due to the fact that this organ has the power of rhythmic contraction. This homologates them with the milk-spots already mentioned. On section they are seen not to invade the substance of the spleen, but to stand up as distinct growths in the capsule. These elevations are of various dimensions, from that of a pin's head to half-a-crown, and are seen to thin off gradually at the edges. When of old standing they frequently undergo calcification.

Microscopically they are composed of lamellated and well-formed fibrous tissue, and are described as lamellar fibromata, or—from their resemblance to the structure of the cornea—corneal fibromata.

Sometimes they are adherent to the parietal peritoneum, just as the milk-spots on the surface of the heart are occasionally united by an organised fibrous tag to the parietal pericardium. But more often, like the cardiac milk-spots, they are free.

Chronic venous congestion of the spleen, such as is often seen resulting from obstructive heart or lung disease, does not give rise to any noticeable enlargement of the organ, as might naturally perhaps be expected. The spleen is hard, firm, of a deep red or purple colour, and about the normal size or slightly enlarged. The capsule is generally somewhat thickened, there is usually an increase of the interstitial supporting tissue—interstitial splenitis—and the venous sinuses are dilated.

In 56 cases of nutmeg liver, all from uncomplicated cases of non-infective heart disease, Dr. Kelynack found the average weight of the spleen to be 7·32 oz.; while in 84 cases of cirrhosis, 53 being males and 31 females, the average weight of the spleen was—males 14·25 oz., females 11·62 oz., or for both sexes together 12·93 oz.

In cirrhosis of the liver the spleen is generally but by no means constantly heavier than normal. In 114 cases of cirrhosis (49) of the liver, of which 47 were fatal from the direct effects of the disease, the remaining 67 dying from independent causes, the average weight of the spleen was 9·8 oz.; taking the normal weight as 7 oz., this shows an increase of 2·8 oz. In the 47 cases of fatal cirrhosis the average weight of the spleen was 11 oz., and in the 67 cases fatal from independent causes 9 oz.; so that the spleen is heavier in cases of active cirrhosis than when this condition is latent. There did not appear to be any constant relation between the weight of the spleen and that of the liver. Price, however, in an analysis of cases of cirrhosis, found large livers and large spleens associated together.

In cirrhosis of the liver—in addition to mechanical venous obstruction, which, as shown by cases of backward pressure due to cardiac or pulmonary disease, is not of itself sufficient to give rise to splenic enlargement—there is frequently a toxic condition of the blood. To this latter factor the splenic enlargement in cirrhosis is probably largely due, for it is